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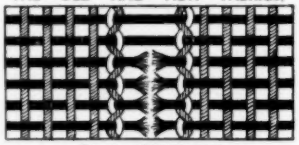

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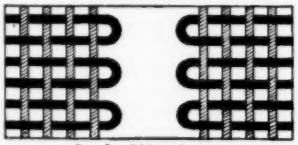

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ADDRESSES AND ORIGINAL ARTICLES

THE MECHANISM OF DIABETES MELLITUS*

BY H. P. HIMSWORTH, M.D. Lond., F.R.C.P.
DEPUTY DIRECTOR, MEDICAL UNIT, UNIVERSITY COLLEGE HOSPITAL, LONDON

I

IN delivering these Goulstonian lectures I shall attempt to fulfil the spirit, if not the letter, of the conditions laid down by Dr. Goulston when in 1632 he made his gift to this college. He directed that his gift should be used to enable one of the younger fellows to demonstrate the results of a disease by dissection of a dead body. My purpose in this and the subsequent two lectures will be to demonstrate the mechanisms of a disease by describing a sequence of experimental observations on the living subject. I can approach this task in no better way than by first describing the clinical observations which originally directed my attention to the significance of one of the most important of these mechanisms.

In the autumn of 1930 I had under my care a woman, aged 30, suffering from severe diabetes mellitus, and I was struck by the fact that, although she would in a short time lose large quantities of sugar in the urine, this loss of sugar from the body did not reduce the blood-sugar level. To test this observation I produced a profuse and periodic diuresis in the patient by giving her quantities of water to drink, and I found that the blood-sugar remained stationary, even though the urinary excretion of sugar varied widely. This observation was the more striking because in the periods of profuse diuresis more sugar would be washed out of the body in half an hour than was contained in the whole volume of the patient's blood, and yet the blood-sugar remained steady at its original level. Pursuing these observations further, I investigated the effect of loss of sugar in the urine on the rise of blood-sugar after the oral administration of glucose. First, the degree of glycosuria and the blood-sugar level in the fasting state were determined, 50 g. of glucose was then given by mouth, and afterwards sufficient water was given to produce a continued diuresis. The sugar content of the blood and that of the urine were estimated at regular intervals. It was found that, although at the end of five hours an excess of 56 g. of sugar had appeared in the urine, the blood-sugar level was still 60 mg. per 100 c.cm. higher than before the glucose had been given. Similar observations were made on other patients and it was further found that the course of the blood-sugar tolerance curve was uninfluenced by the degree of glycosuria (fig. 1). By varying the diuresis the amount of sugar excreted in the urine was varied at different times during the course of the curve, but nevertheless the smooth rise and fall of the curve continued without wavering.[57] To determine if the same significance could be attached to the blood-sugar value in the normal person the same experiments were repeated on persons with renal glycosuria. It is generally conceded that the metabolism in such cases is normal, and that the glycosuria is merely the result of a harmless functional peculiarity of the kidney. Owing to the relatively small loss of sugar in the urine in renal glycosuria the results were not so dramatic as those obtained on diabetics; they were, however, sufficient to show clearly that the course of the blood-sugar in these cases also was not affected by variations in the amount of glycosuria.[57]

These observations appear to me to be very significant. They show that, within the limits of the experiments, the blood-sugar level is uninfluenced by loss of sugar in the urine, even though glycosuria be so profuse that more sugar is removed from the body in the period of observation than is contained in the blood at any particular moment. This can only mean that outflow of sugar into the urine is being actively compensated by an equivalent inflow of sugar into the blood. This observation is incompatible with the old idea that the increased amount of sugar in the diabetic's blood represents a passive accumulation of unutilisable carbohydrate. It suggests that at any particular time the blood-sugar value is fixed by the body at a particular level, and that the maintenance of the blood-sugar at this particular level, whether in the fasting state or in the course of hyperglycæmia, is so important in the metabolism of the body that attempts to change it by physical means are swiftly and accurately countered. The constancy of the fasting blood-sugar level in normal men and animals has been commented on by numerous observers. The failure to realise that under constant dietary conditions the blood-sugar tolerance curve after a dose of glucose also remains remarkably constant [62] can only be attributed to the casual way in which this test is usually performed. For purposes of studying the blood-sugar tolerance accurate curves are necessary, and these require not only that frequent samples of blood be taken but also that the test must be carried out under conditions as strictly controlled as those required for estimation of the basal metabolic rate. All the blood-sugar curves reported in this paper have been carried out under such conditions. The accurate measurement of the blood-sugar tolerance curves thus obtained presented some difficulty until it was found that, although the contour of the curves obtained under constant conditions varied, the area bounded by these curves above the fasting blood-sugar level remained approximately constant.[62] Table I shows that under constant conditions the area of the glucose-tolerance curve remains remarkably constant. It is difficult to believe that such constancy is without significance.

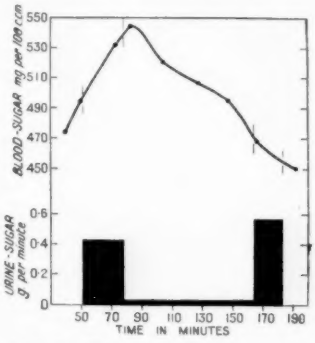

FIG. 1—The curve shows a portion of a diabetic blood-sugar tolerance curve after 50 g. of glucose by mouth; the height of the black area shows the glycosuria in grammes per minutes. The variations in the rate of excretion of sugar do not influence the course of the blood-sugar curve.

* The Goulstonian lectures for 1939 delivered before the Royal College of Physicians of London on March 2, 7, and 9. Lects. II and III, together with the references, will appear in later issues.

Experiments on carbohydrate metabolism in animals provide numerous examples of this maintenance of the sugar in the blood at a particular level; they also provide examples of the disastrous results to the organism when the bodily mechanisms do not maintain this level. From the numerous animal experiments available two illustrative examples may be chosen: (1) the hypophysectomised animal fails to maintain the blood-sugar level partly, if not entirely, because of the diminished inflow of sugar from the liver to the blood; and (2) in phloridzin poisoning the animal fails to maintain the necessary blood-sugar level because of the excessive outflow of sugar into the urine.

(1) When food is withheld from hypophysectomised animals the blood-sugar falls [26 33] and ultimately

TABLE I—CONSTANCY OF THE AREA DEMARCATED BY THE SUGAR-TOLERANCE CURVE WHEN A DIET WITH CONSTANT AMOUNT OF CARBOHYDRATE IS BEING TAKEN

Subject	Diet			Area of glucose tolerance in mg./min.
	Carbohydrate	Protein	Fat	
I	100	80	218	6600 6500
II	50	80	240	9650 9450 8000
III	50	80	240	18,600 15,900
A	250 250 250	80 80 80	100 200 300	3500 3527 3534
B	55 660	88 90	202 42	11,960 13,690 5590 5400
C	55 660	90 90	160 42	11,930 10,660 4160 4550
D	56	87	255	10,890 11,100 10,750

The glucose-tolerance areas were terminated at the shortest time taken by any glucose-tolerance curve on the particular subject to return to normal. The interval between different glucose-tolerance tests on the same diet varied from three days to nine weeks. The figures demonstrate that the greatest discrepancies between duplicate experiments are found when a low-carbohydrate diet is being taken.[66]

death results. It has been shown by Cope [22] that this spontaneous fall of blood-sugar does not take place before the liver-glycogen is practically exhausted. Up to this time the blood-sugar is maintained at normal levels; then, the source of sugar being exhausted, the blood-sugar falls to hypoglycæmic levels. There is strong evidence that in the absence of the hypophysis the ability to manufacture glucose from non-carbohydrate sources and consequently the ability of the starving animal to replenish its liver-glycogen are limited. It is therefore of particular interest that no attempt is made to eke out the supply of liver-glycogen by adjusting the blood-sugar level to markedly subnormal values. Until the liver-glycogen is used up, the blood-sugar is sustained at normal values; then it plunges down to low levels and death results.

(2) After administration of phloridzin to a normal animal, although there are effects on tissues other than the kidney,[103 134] the effects of the excessive glycosuria dominate the picture.[104 142] When phloridzin is given to a fasting normal animal, profuse glycosuria appears and continues for several hours before there is any change in the blood-sugar level. Then the blood-sugar level begins to fall, and, when this happens, it is found that the glycogen in the liver has diminished to minimal amounts. At the same time the increasing excretion of urinary nitrogen indicates an accelerating breakdown of body proteins, while an increasing ketonuria and a fall of the respiratory quotient denote that the body is now driven to obtain its energy mainly if not exclusively from the combustion of fat.[104] The dependance of this sequence of events on the fall of blood-sugar is shown by the effect of the administration of glucose in rapidly restoring the animal to normal.[32] It appears that the fall of blood-sugar which takes place as a result of the excessive glycosuria is of such serious import to the economy of the body that in the attempt to sustain the blood-sugar at normal levels the proteins of the body itself are sacrificed to increase the production of endogenous sugar.

The foregoing results indicate that the fasting blood-sugar levels of the normal and of the diabetic are under given conditions actively maintained within certain levels, and that the degree of alimentary hyperglycæmia, as measured by the blood-sugar tolerance curve, is under given conditions also actively maintained within definite limits. It is extremely unlikely that a constancy of this nature can be fortuitous, and it seems allowable to suggest that the blood-sugar level, in the circumstances existing at any particular time, is that which approaches nearest to the optimum for the needs of the body. This raises two questions: why in different circumstances should the optimal blood-sugar value be fixed at different levels, and how are the changes in optimal blood-sugar level brought about? The consideration of these questions will be facilitated if we anticipate the discussion of some of the evidence that follows and formulate now a working hypothesis. This can then be applied to the experiments as they are presented and its development into a theory followed. Utilisation of sugar by the tissues increases in proportion with the height of the blood-sugar level.[87 126 137 138] It is suggested that the height of the blood-sugar level can be regarded, metaphorically, as a head of pressure of sugar in the blood. In health this head of pressure is within what we recognise as normal limits and ensures that in normal circumstances utilisation of carbohydrate by the tissues proceeds at an adequate rate. If, however, the ability of the tissues to use sugar is diminished—e.g., by either lack of insulin or impairment of insulin action—compensation is made through an appropriate increase in the head of pressure of sugar in the blood. The rate of utilisation of sugar by the tissues is thus maintained relatively constant.[57] Using this hypothesis as a guide, we can now examine the changes in blood-sugar level and the associated alteration in bodily function which take place in normal and abnormal carbohydrate metabolism, and, if this guide prove to be true, we can hope eventually to construct a theory which renders these changes and their associated alterations intelligible.

SIGNIFICANCE OF VARIATIONS IN THE BLOOD-SUGAR LEVEL

We can best approach the question of why the blood-sugar level varies by considering the effects of manipulating the height of the blood-sugar level on sugar utilisation and on insulin action. The effect of the blood-sugar level on sugar utilisation in normal animals is well established. After ingestion of glucose the respiratory quotient and the consumption of oxygen rise, and Lusk [87] has explained this effect

as due to the plethora of glucose in the blood increasing utilisation of sugar. More recently Wierzuchowski [137 138] has shown that in normal animals the assimilation and oxidation of ingested glucose increase with the rate of its infusion and the rise of blood-sugar up to a high limiting value. Increase in the height of the blood-sugar level similarly favours the action of insulin in normal subjects.[55 61 66 119] Under constant conditions of diet the higher the level of the fasting blood-sugar the greater the effect of a standard dose of insulin in depressing the blood-sugar. This relation between fasting blood-sugar level and insulin effect has been closely investigated by Scott and Dotti,[119] who have shown that the effect of a standard dose of insulin in depressing the blood-sugar is proportional to the height of the fasting blood-sugar level on which it acts. Recently Dr. R. B. Kerr and I [66] have shown that a similar relationship governs the action of insulin in suppressing alimentary hyperglycæmia. Under constant dietary conditions the greater the glucose-tolerance curve the greater the effect of a standard dose of insulin in suppressing the glucose-tolerance curve. It thus appears that, when the head of pressure of sugar in the blood is high, sugar utilisation and insulin action are facilitated, whereas, when the head of pressure of sugar is low, sugar utilisation and insulin action are retarded. In healthy subjects the fasting blood-sugar level varies relatively little. The blood-sugar tolerance curve of healthy subjects, however, varies widely according to the different conditions under which it is obtained, and consideration of these variations and of the phenomena associated with them throws considerable light on the purpose behind their changes.

ASSOCIATION BETWEEN INSULIN SENSITIVITY AND GLUCOSE TOLERANCE

It was noted by Claude Bernard [11] that when a carbohydrate-rich meal was given to a starving dog glycosuria often followed. In 1913 Bang [9] showed that starvation caused a high blood-sugar tolerance curve—i.e., lowered the tolerance of the animal for glucose. Later Adlersberg and Porges [2 3] and Sweeney [129] showed that high-fat diets caused a high tolerance curve, whereas high-carbohydrate diets caused a low tolerance curve. I have shown

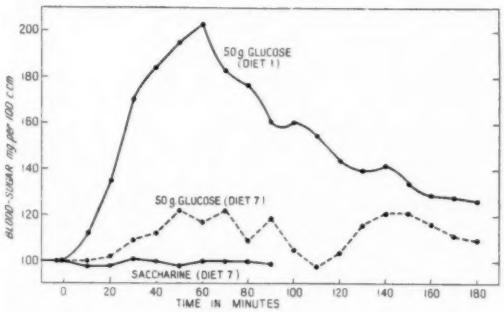

FIG. 2—Three blood-sugar curves from the same healthy subject. The curve on diet 1 shows the effect of a low-carbohydrate diet on the glucose-tolerance curve produced by oral administration of 50 g. glucose; the curve on diet 7 shows the effect of an equicaloric high-carbohydrate diet. The saccharine curve is a control experiment showing that no rise of blood-sugar follows the drinking of a solution of saccharine or is caused by the experimental technique.[62]

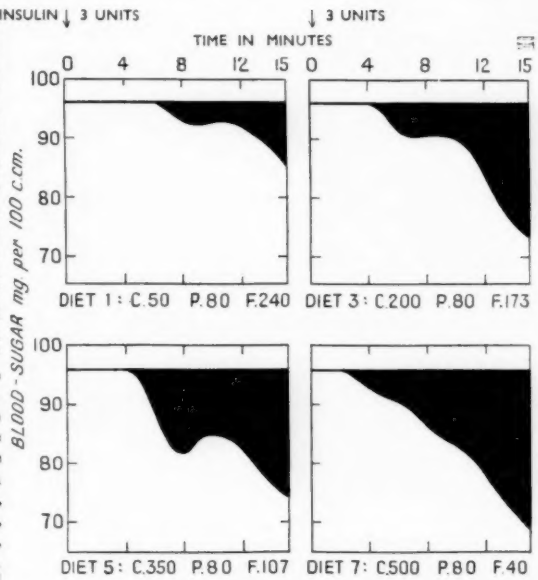
INSULIN ↓ 3 UNITS
↓ 3 UNITS
TIME IN MINUTES
BLOOD-SUGAR mg per 100 c.cm.
DIET 1: C.50 P.80 F.240
DIET 3: C.200 P.80 F.173
DIET 5: C.350 P.80 F.107
DIET 7: C.500 P.80 F.40

FIG. 3—Four insulin-depression curves, after injection of 3 units of crystalline insulin solution intravenously, obtained from the same healthy subject when taking diets containing different amounts of dietary carbohydrate.[62]

that the sole dietary factor governing sugar tolerance is the absolute amount of carbohydrate in the preceding diet; with progressive restriction of dietary carbohydrate there is progressive impairment of sugar tolerance, which is shown by a corresponding heightening of the blood-sugar tolerance curve.[62] The results in a typical experiment are shown in fig. 2, and a series of such curves measured by the method of areas is shown in table I. It will be seen that, while the size of the areas depends on the composition of the preceding diet, repeated tests under constant dietary conditions show a remarkable degree of constancy. It is therefore possible to vary the height to which the blood-sugar rises after ingestion of a constant dose of glucose by varying the carbohydrate content of the preceding diet; but, if the dietary carbohydrate is maintained constant, the blood-sugar tolerance curve remains constant also.

The action of insulin in depressing the blood-sugar level in normal and diabetic subjects is perhaps its most characteristic effect, and it is now realised that this action is not fixed but can be varied. When in the second of two tests the same dose of insulin depresses the blood-sugar more rapidly than in the first, the insulin sensitivity of that subject is said to have increased. It should be emphasised that the term "insulin sensitivity" applies only to the rate at which the blood-sugar is depressed. The speed of return to normal levels is irrelevant, depending on factors other than insulin action. The rate at which a standard dose of insulin depresses the fasting blood-sugar level depends on the composition of the preceding diet [1 8 62 131] and, as in the case of the glucose-tolerance curve, it is the carbohydrate content of this diet which is the determining factor. With progressive restriction of dietary carbohydrate there is progressive diminution in the effect of a standard

dose of insulin on the fasting blood-sugar level, with the result that the blood-sugar is depressed more slowly and to a less extent, and the area traced out by the insulin-depression curve below the fasting blood-sugar level diminishes.[62] A typical experiment is given in fig. 3, which shows that, as the carbohydrate content of the diet is increased, the sensitivity of the subject to insulin increases, with the result that each unit of insulin disposes of more sugar in a given time. Thus increasing the dietary carbohydrate has a twofold effect: it improves the blood-sugar tolerance curve, and it improves the sensitivity to insulin. This association appears to be invariable. Before, however, considering why these changes in the sugar-tolerance curve are correlated with similar changes in insulin sensitivity it is necessary first to consider if the variations in sugar tolerance resulting from dietary changes can be explained by variations in the secretion of pancreatic insulin.

Closely related to the effect of dietary carbohydrate on the sugar-tolerance curve is the phenomenon first described by Hamman and Hirschmann,[53] who showed that periodic ingestion of constant amounts of glucose led to progressively smaller rises of the blood-sugar. This work has been confirmed and extended by Staub[128] and by Traugott,[132] by whose names the phenomenon is now usually known. The accepted explanation of the Staub-Traugott phenomenon is that each successive dose of glucose provokes an increased secretion of insulin. At first sight the explanation appears very probable, for there is considerable evidence that a rise of blood-sugar is an adequate stimulus to the secretion of pancreatic insulin. Soskin et al.,[121] however, have shown that in a depancreatised dog, receiving a constant injection of insulin sufficient to maintain its blood-sugar at normal levels, the periodic injection of constant doses of glucose still leads to progressively smaller rises of blood-sugar. The progressive improvement in sugar tolerance can thus be explained without postulating a progressive increase in the secretion of pancreatic insulin. Studying the same phenomenon I showed that repeated injections of glucose caused a corresponding increase in the insulin sensitivity of the animal.[61] It therefore appears that the Staub-Traugott phenomenon must be explained not as the result of a progressively increasing secretion of endogenous insulin but as the effect of a constant amount of insulin in the presence of a progressively increasing sensitivity to insulin.

The correlation between the changes in glucose tolerance and in sensitivity to insulin induced by change in the carbohydrate content of the diet has been indicated above. On closer examination this correlation is found to be surprisingly exact. If the effects of several diets differing in carbohydrate content are tested on the glucose-tolerance curve and on the insulin-depression curve, it is found that changes in glucose tolerance are accurately correlated with proportionately equal changes in sensitivity to insulin. In other words, dietary changes in glucose tolerance can be adequately accounted for by changes in the sensitivity of the subject to his own pancreatic insulin.[62] This conclusion carries an implication which accords with the experiments of Soskin quoted above: that the amount of insulin secreted by the normal pancreas in response to ingestion of a standard dose of glucose is constant; and it suggests further that the secretory response of the islets of Langerhans to a plethora of glucose is of the "all or none" type.

It is now possible to see a purpose underlying the variations in the glucose-tolerance curve which result from changes in dietary carbohydrate. It has been shown that under constant conditions the effect of insulin in depressing the fasting blood-sugar level, or in suppressing the rise of blood-sugar after ingestion of glucose, increases with the height of the blood-sugar. After restriction of dietary carbohydrate the sugar-tolerance curve rises to levels higher than normal. Under the same conditions sensitivity to insulin is depressed. It will be seen that this change in the sugar-tolerance curve is such that it tends to counteract the effect of diminished sensitivity to insulin. When insulin sensitivity becomes impaired, there is a compensatory increase in the head of pressure of sugar in the blood during the course of the sugar-tolerance curve. This facilitates the action of insulin on the blood-sugar, with the result that the effect of the insulin secreted by the pancreas remains unimpaired. Direct evidence in favour of this view has recently been obtained.[66] It was found that, when insulin sensitivity was constant, the effect of a standard dose of insulin in suppressing the glucose-tolerance curve was proportional to the height of the curve on which the insulin acted. Now, the size of the blood-sugar tolerance curve can be varied by varying the carbohydrate content of the preceding diet, but this procedure also changes the sensitivity to insulin. In each of the different conditions of insulin sensitivity produced it was found that the effect of a standard dose of insulin in suppressing the blood-sugar curve remained constant and was no longer proportional to the height of the curve. Thus the same amount of blood-sugar was removed by the standard dose of insulin when the curve was high and the sensitivity to insulin low as when the curve was low and the sensitivity to insulin high. The increased head of pressure of sugar in the blood had compensated the diminished sensitivity to insulin. If the conditioned variations in the blood-sugar which we have been considering have as their object the neutralising of the effect of changes in insulin sensitivity, it is important to know what would be the effect of such variations in sensitivity to insulin if no such neutralising mechanism existed.

INSULIN SENSITIVITY AND THE UTILISATION OF BLOOD-SUGAR BY THE PERIPHERAL TISSUES

The peripheral action of insulin was clearly demonstrated by Mann and Magath[94] and by Burn and Dale.[18] Mann and Magath showed that after hepatectomy in dogs insulin produced a fall of blood-sugar comparable with that observed in normal animals; and Burn and Dale demonstrated that insulin caused the disappearance of large quantities of infused sugar in decapitated eviscerated preparations. This work was extended by the experiments of Frank, Nothmann, and Wagner,[46] who showed that injection of insulin, both in the intact and in the depancreatised dog, caused an increase in the abstraction of sugar from the blood, as shown by an increase in the arteriovenous (A-V) sugar difference, and moreover that after intra-arterial injection of insulin the A-V sugar difference was most obvious in the limb supplied by that artery. There is now no doubt that the action of insulin in the peripheral tissues is not constant but depends on other factors. It has been shown, for example, that after treatment with extracts of the anterior-pituitary gland the action of insulin is greatly reduced both in promoting deposition of muscle-glycogen in eviscerated preparations[88] and in accelerating the fall of blood-sugar in rabbits in which the liver is excluded.[69] Direct evidence that the carbohydrate content of the preceding diet influences the uptake of sugar by the peripheral

tissues has been brought forward by Drury [34] and endorsed by Mann. [92 93] These authors have found that after hepatectomy the spontaneous fall of the blood-sugar is faster, and the amount of sugar that must be infused to keep the blood-sugar constant is greater, when the animals have previously received a diet rich in carbohydrate than when they have been starved. This work has been denied by Soskin,[123] but it is doubtful if his preparations were suitable for investigation of the delicate variations in the peripheral uptake of sugar as a result of dietary changes. It thus appears that conditions which diminish sensitivity to insulin also diminish the ability of the peripheral tissues to utilise the blood-sugar.

In the intact animal or human subject the only method available for studying the rate of removal of sugar by the peripheral tissues is to measure the difference between the sugar content of the arterial blood entering a limb and that of the venous blood leaving the limb.[45] An increase in this A-V sugar difference indicates an increased rate of removal of sugar by the peripheral tissues. A diminished A-V sugar difference is found in depancreatised dogs [46] and in human cases of diabetes mellitus,[92a] and this difference is restored to normal by injection of insulin. In a normal subject the A-V sugar difference in the resting state is small, but after ingestion of sugar the difference increases as the blood-sugar rises, and then decreases to the fasting value as the blood-sugar falls.[60] This increase in the A-V sugar difference is attributed to the action of the pancreatic insulin secreted in response to the rise of blood-sugar, and the effect of this pancreatic insulin in causing the peripheral tissues to remove the blood-sugar can be measured by the area enclosed between the arterial and the venous blood-sugar tolerance curves. In fig. 4 is shown an example of two experiments on the same healthy subject, in which after ingestion of a standard dose of glucose both capillary and venous blood-sugar curves were estimated. In one experiment the subject was taking a low-carbohydrate diet; in the other a high-carbohydrate diet. The area enclosed between the capillary and venous blood-sugar curves is the same in each case, indicating that the removal of sugar by the peripheral tissues was the same in both experiments. But according to the results on hepatectomised animals the peripheral tissues should have removed less sugar from the blood when the subject was taking a low-carbohydrate diet than when he was taking a high-carbohydrate diet. It has already been shown, however, that the removal of sugar from the blood increases as the head of pressure of sugar in the blood rises. It thus appears that in the above experiments, when the low-carbohydrate diet was being taken, the diminished ability of the peripheral tissues to remove sugar was compensated by the increased height to which the blood-sugar rose, with the result that the action of the pancreatic insulin in promoting removal of sugar from the blood by the peripheral tissues remained the same as when the subject was taking a high-carbohydrate diet. The evidence thus points to insulin sensitivity being a phenomenon of the peripheral tissues and indicates that the purpose underlying the variations in the blood-sugar tolerance curve resulting from dietary changes is to maintain relatively constant the supply of sugar to the peripheral tissues.

So far as is known, the main consumption of sugar takes place in the extrahepatic tissues, and it might therefore be expected that, if insulin sensitivity is a phenomenon of these tissues, wide variations in insulin sensitivity would be associated with detectable variations in the oxidation of sugar. The most important work in this field is that of Dann and Chambers [30] on the effect of starvation on the specific dynamic action of glucose. When glucose is given orally to a dog, the increased oxidation of sugar is indicated by a rise both in the consumption of oxygen and in the respiratory quotient. In dogs starved for three weeks this effect of glucose is greatly reduced. At the time when this work was done it was generally accepted that starvation decreased the output of pancreatic insulin. The work we have been considering, however, shows that it is the sensitivity to insulin

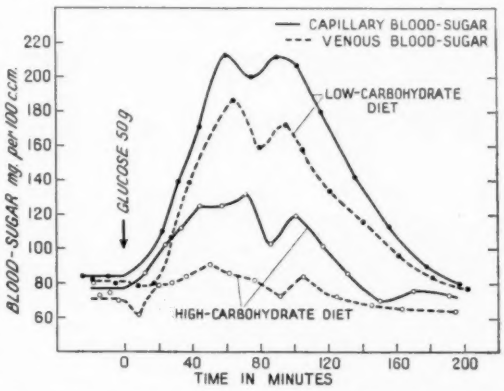

FIG. 4—Two experiments in the same healthy subject, showing the rise of capillary blood-sugar and the rise of venous blood-sugar after ingestion of 50 g. of glucose. Before one experiment the subject was taking a low-carbohydrate diet; before the other a high-carbohydrate diet. The area enclosed between the capillary and venous blood-sugar curves indicates the amount of sugar removed from the blood by the peripheral tissues. The areas are approximately equal in both experiments.[60]

which is decreased by starvation, and it is therefore significant that Dann and Chambers found that large doses of insulin did not restore to normal the ability of the starved dog to oxidise carbohydrate. These workers showed, however, that the oxidation of glucose in dogs could be restored to normal in three or four days by repeated administration of glucose, a measure which increases the degree of sensitivity to insulin. In man Baur [10] found that the consumption of oxygen by men receiving a low-carbohydrate high-fat diet was significantly lower than when they were taking a high-carbohydrate low-fat diet. This finding has been confirmed, but it also appears that after ingestion of glucose the resulting rise in the respiratory quotient indicates that the proportion of the ingested glucose oxidised when taking either of the two diets is not greatly different.[27] Thus restriction of carbohydrate coincidentally impairs insulin sensitivity and ability to oxidise glucose, whereas administration of carbohydrate restores both these properties. When the sensitivity to insulin is moderately decreased, as by simple restriction of dietary carbohydrate, the coincidentally decreased ability to oxidise carbohydrate is compensated. When, however, insulin sensitivity is much impaired, as by prolonged starvation, the compensation may be inadequate, and ingestion of glucose may not produce the full normal increase in metabolism.

The importance of insulin sensitivity in carbohydrate metabolism is now apparent. Decrease in

insulin sensitivity, if uncompensated, leads to diminished utilisation of sugar. To counteract this diminution of sugar utilisation the blood-sugar curve is elevated and the head of pressure of blood-sugar thereby increased. As a consequence of this increased head of blood-sugar pressure the action of the insulin secreted by the pancreas is facilitated. The impaired sensitivity to insulin is thus compensated, with the result that the rate of utilisation of sugar by the tissues is maintained within relatively normal limits (table II). This problem of insulin sensitivity has

TABLE II—EFFECT OF CHANGE IN INSULIN SENSITIVITY

Insulin sensitivity	Effect	Compensation	Result
Diminished	(*a*) Insulin action impaired (*b*) Utilisation of sugar impaired	Increase in height of blood-sugar	Sugar utilisation approximately normal
Increased	(*a*) Insulin action increased (*b*) Utilisation of sugar increased	Decrease in height of blood-sugar	Sugar utilisation approximately normal

been considered in some detail because it provides an excellent example of the reaction of the body when its ability to utilise carbohydrate is impaired. These reactions take place in the healthy subject and cannot be considered abnormal. When we come to consider the diseases in which ability to utilise carbohydrate is impaired, we shall see that these same reactions are much in evidence. The thesis which I shall then be concerned to develop is that these reactions, particularly the hyperglycæmia of diabetes mellitus, are not abnormal processes, deleterious in themselves, but manifestations of an attempt to compensate the impaired ability of the tissues to utilise carbohydrate.

A NEW SERUM IN THE PASSIVE CONTROL OF SCARLET FEVER

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It is difficult to know how far one is justified in recognising scarlet fever as a disease per se rather than as one of the results of infection of the upper respiratory tract by certain strains of hæmolytic streptococci. That the latter view is fundamentally correct has long been apparent on clinical and epidemiological grounds, but conclusive proof was not forthcoming until the introduction by Griffith (1934) of the serological classification of the hæmolytic streptococci. The hæmolytic streptococci concerned are chiefly the many serological types which fall into Lancefield's group A and need not be further particularised here. The clinical condition caused by infection with such an organism depends partly on the site of the infection—e.g., upper respiratory tract, genital tract in the puerperium, and wounds—and partly on the immunological condition of the person infected. With an infection of the upper respiratory tract in the absence of circulating antibody to the erythema (Dick) toxin, scarlet fever develops; when the specific antibody is circulating in sufficient concentration the toxin is neutralised, the rash does not appear, and the diagnosis is tonsillitis, septic sore-throat, or the like. It follows that such infections or their complications—e.g., otitis media, rhinitis, and mastoiditis—may produce secondary cases of scarlet fever if transmitted to Dick-positive subjects. Similarly, hæmolytic streptococcal "colds," infected wounds, or discharges may be responsible for secondary cases of scarlet fever.

The rational method of classifying these infections is evidently bacteriological rather than clinical, as in enteric and pneumococcal infections. Administratively, however, scarlet fever is still an entity, since it is a notifiable disease, whereas its congeners (other than erysipelas and puerperal infections) are not. Moreover, in communities containing a relatively large proportion of Dick-positive reactors it is likely to be the most frequent manifestation of hæmolytic streptococcal infections of this type. Thus in the wards of a children's hospital, where commonly half or more of the patients are Dick-positive, scarlet fever constitutes the most striking evidence of the existence and spread of cross-infection with this group of organisms.

Like many other hospitals, the old Hospital for Sick Children admitted septic otorhinological cases to a general surgical ward. Such a ward offers considerable opportunity for cross-infection with hæmolytic streptococci (Okell and Elliott 1936) and is likely to present an undue number of cases of scarlet fever. By dint of careful barrier nursing the number of cases of scarlet fever was kept commendably low, the figures being:—

1934	.. .. 5 cases	1936	.. .. 3 cases
1935	.. .. 9 „	1937 (1st half)	.. 4 „

Pending the opening of new wards with adequate isolation accommodation, it was decided to administer scarlet-fever antitoxin prophylactically to all cases on admission to this ward, in an attempt to reduce still further the number of cases of scarlet fever.

EXPERIENCE WITH EARLIER SERUM

The successful routine use of a serum prophylactically on such a scale depends not only on its efficacy as a preventive but also on its liability to cause serum reactions. Although ad-hoc records had not been previously kept, the opinion was held at Great Ormond Street that the commercial scarlet-fever sera then in use at the hospital were reliable prophylactics but caused serum reactions in an undue proportion of patients. These reactions, although very rarely dangerous, were often severe and interfered with the well-being and treatment of the patients.

The proportion of patients exhibiting reactions after the injection of sera in general varies from one batch of serum to another; with individual sensitivity; but especially according to the amount of protein injected. The most recent published figures agree remarkably closely: 21·9 per cent. for diphtheria antitoxin (Davis 1938); 28·1 per cent. for diphtheria antitoxin and 22·7 per cent. for scarlet-fever antitoxin (Hunt 1932). At Great Ormond Street one had the impression that stock scarlet-fever antitoxin used in 5 c.cm. doses gave a substantially higher figure, some batches giving reactions in quite half the patients.

TECHNIQUE AND RESULTS WITH REFINED SERUM

It was therefore decided to give a trial to the scarlet-fever antitoxin introduced by Lederle Laboratories. According to the makers, these sera are refined and concentrated by a process of "selective and controlled digestion of the inactive, reaction-producing proteins by means of proteolytic enzymes."

The sera are said to contain the pseudoglobulin fraction only and are claimed to give a very low incidence of serum reactions. The dosage recommended for passive protection against scarlet fever is 1–1·5 c.cm. (100,000 original neutralising units). Past experience with other sera suggested that this dosage was excessive for our purpose, for the patients at Great Ormond Street are all under twelve years of age. Accordingly a routine dosage of 0·75 c.cm. (75,000 original neutralising units) was employed. Babies under four months of age were not injected, for they are usually Dick-negative.

Most patients received their serum within a few hours of admission and virtually all within twenty-four hours. A few patients remaining in the ward for periods of only a few hours did not receive serum. The serum was given intramuscularly in the deltoid region or thigh indifferently. No distinction was made between patients receiving serum for the first time and those who had had serum on a previous occasion. The ward-sister and her nurses were instructed to report all disturbances, however slight, which might conceivably be referable to the administration of serum.

The period during which serum was thus given as a routine was from July 27, 1937, to Aug. 4, 1938 (just over a year), and 658 patients received the serum. During the course of the trial 1 case of scarlet fever developed in the ward. This case cannot be recorded as a failure of the serum to protect in that the child had been forty-eight hours in the ward before the administration of serum and that signs of scarlet fever appeared within a few hours of the injection.

The serum has also been employed in the control of scarlet fever in the general medical and surgical wards. The method of dealing with scarlet fever in these wards has been (1) immediate removal of the primary case, (2) Dick-testing of all contacts, and (3) the administration of Lederle serum 0·75 c.cm. to all positive reactors within twenty-four hours of the diagnosis of the primary case. During the period under review there have been 14 primary cases of scarlet fever in the general wards, involving 135 Dick-positive contacts. They were dealt with as above, and no secondary case developed.

As is so often the case in human protection experiments, there is no means of estimating how many susceptibles did in fact make effective contact and therefore would have developed scarlet fever if not passively protected. Obviously efforts were made to make the number as small as possible. The results in the otorhinological ward, where no case of scarlet fever developed during the twelve months in which routine serum was given as against 3–9 cases in the previous years, are no doubt within the range of chance variation. The results obtained in the general wards are certainly not open to this criticism.

Less favourable results have been obtained by Dr. McSweeney at the Cork Street Fever Hospital, Dublin. He has had several failures to protect when using Lederle serum to control the introduction of scarlet fever to diphtheria wards. The conditions in his series were less favourable in that they were cases "whose resistance was at a very low ebb, exposed to pretty intensive infection with hæmolytic streptococci" (McSweeney 1939). There is also the possibility that the serum may not be equally effective against every type of scarlatinal streptococcus.

The number of patients recorded as showing serum reactions is 10 out of a total of 793 receiving serum—i.e., 1·2 per cent. In 2 of the cases the reaction was local only; in the remainder there were general reactions, usually with an urticarial type of rash. It is probable that a few cases developed reactions after discharge from hospital; but, even when allowance is made for this source of error, the percentage of reactions is remarkably low, especially when it is remembered that no precautions were taken in reinjecting patients who had had serum previously.

SUMMARY

A new scarlet-fever antitoxin (Lederle Laboratories) has been tested as a means of passive prophylaxis in the wards of a children's hospital.

Secondary cases were practically abolished during the year in which it was used.

In prophylactic doses it gave rise to serum reactions in less than 2 per cent. of cases.

My thanks are due to the members of the honorary staff to whose cases these figures relate and to Dr. D. N. Nabarro, director of the pathological department, for much help and advice. The work was done during the tenancy of a grant from the Sir Halley Stewart Trust.

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THE ÆTIOLOGY OF POLYARTHRITIS IN THE RAT

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IN a number of papers Collier (1938 and 1939a, b) and Collier and Esseveld (1938), working in Java, have reported on a spontaneous polyarthritis of rats which can be transmitted in series, but of which the ætiological agent has not been isolated. A very similar condition was demonstrated to one of us in 1930 in Nigeria by Mr. R. S. Marshall, M.R.C.V.S., whose observations have not yet been published. A closely allied condition has been found in rats in our own laboratory and in the rat colonies of two other laboratories in London. The object of the present communication is to show that the causal agent of this disease is a pleuropneumonia-like organism.

THE SPONTANEOUS DISEASE

The disease has been seen in pure-bred black and white rats and in albino rats of the Wistar strain. The joints most commonly affected are the tibiotarsal and the radiocarpal; less frequently the intertarsal or phalangeal joints are swollen. In the spontaneous disease, it is not uncommon to see three or all four of the limbs involved. The first signs of swelling of an affected joint are accompanied by a glistening appearance of the skin, which is smooth and pearl-coloured. Often these appearances are localised to one small nodule. Later the whole region of the joint takes on a pink and even purplish tint and is slightly œdematous. This condition may eventually subside, leaving some thickening round the

joint; or, while the joint is still swollen, the skin may ulcerate and the limb below the joint may be gnawed off by the rat. The skin can be easily stripped off affected joints in the early stages, showing in the case of the tibiotarsal joint a fusiform swelling, of a pearly colour. On cutting the swollen tissues, straw-coloured fluid may be liberated.

Attempts to transmit the disease were made by removing the skin from affected joints with aseptic precautions and grinding up the whole joint with sterile sand. Normal saline was then added to make an approximately 10 per cent. suspension and, after centrifugation at 3000 r.p.m. for 10 minutes, the supernatant fluid was inoculated into the pad of the hind foot of half-grown rats in doses of 0·2 c.cm. The first symptoms appeared usually in the tibiotarsal joints, more rarely in one of the intertarsal joints, after an interval of 4–6 days. In very large rats the incubation period was as long as 10 days, while certain full-grown rats showed no symptoms of infection.

ISOLATION OF A PLEUROPNEUMONIA-LIKE ORGANISM

Smears from affected joints showed the presence of large numbers of polymorphonuclear leucocytes and on occasions bacteria. Histologically, in the early stages, there was infiltration round the joint with polymorphonuclear leucocytes and large mononuclear cells. Later, fibroblasts appeared and what suggested pannus formation was noted. Finally the joint cavity was invaded, with disappearance of articular cartilage and absorption and disorganisation of the epiphysis.

The first step in the attempted isolation of the causal agent was the filtration of the affected joint tissues. A 10 per cent. suspension having been centrifuged as before, the supernatant fluid was filtered through gradocol membranes with A.P.D. of 940 mμ, 790 mμ and 680 mμ under a pressure of 3 atmospheres of nitrogen. The filtrates were then inoculated in doses of 0·2 c.cm. into the pads of half-grown rats together with a small amount of sterile agar: cultured on ordinary bacteriological media the filtrates showed no growth. Six to eight days after inoculation the tibiotarsal joints of the rats began to swell and a week later the joints were very definitely affected. Attempts at culture were made from joints thus infected by filtrates. No growth was obtained on the more commonly employed bacteriological media, but when agar or broth containing about 20 per cent. of defibrinated rabbit blood was employed, or when joint fluid was spread on Klieneberger's "special medium," growth was obtained of an organism whose growth characteristics and morphology resembled those of other pleuropneumonia-like organisms, more especially the organism which we have termed L5 (Findlay et al. 1938).

These agar and broth cultures, with the addition of sterile agar, when injected into the pads of rats caused swelling of the tibiotarsal joints after an interval of 4–6 days, and the appearance of the same symptoms as are caused by the injection of a suspension of the affected tissues. Histologically, the experimental does not differ from the spontaneous disease. Polyarthritis may occur in the experimental disease. Thus in one instance a rat inoculated into the pad of the right hind foot developed an acute arthritis of the left knee-joint 16 days later. Injected intravenously in rats of 50 g. body-weight in doses of 0·5 c.cm. fluid cultures induce polyarthritis in 5–8 days.

The pleuropneumonia-like organism, which is provisionally termed L7, is present in affected joints for considerable periods. During the acute stage it can be obtained in small amounts from the heart blood, popliteal lymph-nodes and spleen. L7 has been cultivated on the chorio-allantoic membrane of the developing chick embryo and reinoculation of the infected membranes in the pads of rats causes typical arthritis. Intracerebral injection of cultures in rats as a rule causes no symptoms, but in one instance a rat was moribund 4 days after injection. The brain of this rat contained the organism which further observation shows may remain latent in the brain for considerable periods, certainly up to 21 days.

Attempts have been made to infect species other than the rat.

Injection of agar cultures of L7 in the knee-joint of pigs was without effect, while injection in the pad of the foot of rhesus and cercopithecus monkeys and of rabbits, voles, guineapigs and hedgehogs produced no rise of temperature and no swelling of the joints. Injection of either infected filtered material from the rat or cultures of L7, mixed with agar, into the pads of mice gave rise, however, to swelling of the tibiotarsal joint in 2–7 days: the swelling may persist for 5–6 weeks. Without the addition of agar, little or no reaction is produced in mice. In some mice injection of cultures into the pad causes also a gelatinous œdema of the subcutaneous tissues of the abdominal wall, followed by death. Cultures of L7 on agar have also been injected intracerebrally into mice and give rise in 2–7 days to a fatal condition, associated with weakness in the hind legs, hunched back, coarse tremor and a tendency to turn in circles with the tail as a fixed point. Not infrequently, the skin over the frontal region becomes thickened, indurated and the eyes may be closed by a sticky exudate. In the first passage only one or two mice may show symptoms, but repeated passage, especially with the addition of sterile agar, causes 60–80 per cent. of the mice to develop cerebral symptoms. Histologically no lesions are seen in the brain beyond a slight degree of meningitis.

Cultures inoculated intravenously or intraperitoneally in doses of 0·5 c.cm. cause death in a high percentage of animals. In those that survive for 48 hours pleural or peritoneal exudates and arthritis are common. Intranasal instillation causes pneumonia in 5–8 days.

Smears from the brains of inoculated mice show the presence of large numbers of polymorphonuclear leucocytes and of rings, granules and comma-shaped structures which we have learnt to associate with infection by pleuropneumonia-like organisms isolated by us from mice (Findlay et al. 1939). Similar bodies have been seen in rat brain inoculated with agar cultures, in the chorio-allantoic membrane of the chick embryo, and in blood-broth cultures 24 hours after inoculation. They exhibit certain morphological similarities to the parasite known as *Eperythrozoon coccoides* and found in the blood of splenectomised mice. Like them the bodies stain readily by Giemsa's method and give a positive Feulgen reaction for nucleic acid. It seems that all pleuropneumonia-like organisms require an adjuvant such as agar or cells to start infection, if injected into animals. Mettam and Ford (1939), adopting Daubney's method (1936), demonstrated this recently in experiments on cattle with pleuropneumonia itself, and previous observations (Findlay et al. 1938) have emphasised its importance in regard to pleuropneumonia-like organisms in rodents. Collier (1939b) was unable to produce polyarthritis in mice.

Collier (1939a) showed that the injection into rats of certain organic gold preparations, Aurodetoxin

and Solganal B, prevented the development of polyarthritis in rats: we have now been able to confirm and extend his results with solganal B by showing that this compound prevents the development of arthritis in both rats and mice injected with cultures of the pleuropneumonia-like organism L7. Solganal B and other organic gold compounds also have a very remarkable effect in preventing symptoms in mice injected intracerebrally with L4, L5 and L6, other pleuropneumonia-like organisms isolated from rats and mice.

RELATIONSHIP OF L7 TO OTHER PLEUROPNEUMONIA-LIKE ORGANISMS

During the past few years observations have shown that the group of pleuropneumonia-like organisms is very widely distributed. On the one hand, saprophytic agents such as those described by Laidlaw and Elford (1936) and Seiffert (1936 and 1937) in sewage, humus, earth and similar materials undoubtedly belong to this group, as do the agents responsible for pleuropneumonia in cattle and agalactia in sheep and goats. Incidentally, it is of interest to note that arthritis is by no means uncommon in goats affected with agalactia. According to Pigoury (1938) arthritis occurs in 10–20 per cent. of these animals, coming on usually about a week after the beginning of the disease. One joint alone is as a rule attacked, generally that between the radius and the carpus, more rarely the tibiofemoral or the tibio-astragaloid joint. The symptoms vary from simple stiffness to acute arthritis with complete functional incapacity. Spontaneous cure usually takes place after one or two months, but in some cases ankylosis is complete. Serous inflammation of the joints is occasionally described as a late symptom in pleuropneumonia of cattle.

At least four different species of pleuropneumonia-like organisms have been isolated from mice. L1 obtained from mice and rats is associated with *Streptobacillus moniliformis* (cf. Klieneberger 1936 and 1938). This organism may occasionally produce arthritis in mice. L3 has been found in the lungs of rats suffering from "bronchopneumonia" (cf. Klieneberger and Steabben 1937) and has recently been isolated from the brain of an apparently healthy mouse. L5 was isolated from the brains of mice showing curious nervous symptoms—rolling disease (Findlay et al. 1938): a very similar organism was subsequently identified by Sabin (1938) as the causal agent of a similar condition in America. In America, Sabin (1939) has also isolated a pleuropneumonia-like organism from the brain of an apparently normal mouse. Both L5 and this latter organism may produce an arthritic condition in mice when injected intraperitoneally or intravenously in large doses. In this country, Findlay et al. (1939) have also obtained on numerous occasions from mouse brains a pleuropneumonia-like organism L6, which differs from L5 serologically and in its growth characteristics. This organism is also capable of producing arthritis in about 30 per cent. of mice. In rats, Woglom and Warren (1938a and b) described a pyogenic condition which they at first regarded as due to a filtrable virus. This has now been shown by Klieneberger (1939) and Woglom and Warren (1939) to be due to a pleuropneumonia-like organism L4, which is quite distinct from the mouse pleuropneumonia-like agents. L4 can, however, be adapted to mouse brains. Recently Swift and Brown (1939) claim to have isolated from exudates and skin nodes in rheumatic fever in man a pleuropneumonia-like organism which they have been able to grow on the chorio-allantoic membrane of eggs and have also passaged in mice.

Attempts have been made to compare L7, the organism isolated from rat polyarthritis, with other pleuropneumonia-like organisms obtained from rodents. When L5 and L6 are injected into the pads of rats no arthritis results and the symptoms on intracerebral injection in mice are different. L4, injected into the pad of rats and mice, produces an arthritis indistinguishable from that caused by L7, but its pathogenicity for mouse brains is greater than that of L7, while smears from the brains of mice infected with L4, although revealing structures not unlike virus elementary bodies, have shown no rings similar to those produced by L5, L6 and L7. L4, however, produces the same infiltration of the skin of mice following intracerebral inoculation. L7, injected subcutaneously into rats, causes no formation of pus as does L4. In its growth characteristics on solid media L7 resembles in certain respects L5, though it develops more slowly. Mice immune to L5 and L6 can be infected with L7.

Further work, however, is required to determine the exact relation of L7 to other pleuropneumonia-like organisms of rodents. L7 is killed after heating for 30 min. at 50° C. It passes gradocol membranes with A.P.D. of 560 mμ and 440 mμ but not 300 mμ. It can be preserved in 50 per cent. glycerin saline for 22 days: it resists freezing and drying and a 0·5 per cent. solution of phenol for at least a week at 4° C. The greater part of a suspension is sedimented after centrifugation at 15,000 r.p.m. for two hours.

DISCUSSION

The spontaneous infectious polyarthritis which we have described in rats in London appears to be identical with, or very closely related to, the condition observed by Collier (1938) in Batavia except that his condition was not transmissible to mice. It also resembles the condition observed by Marshall in Nigeria, referred to above, in a stock of laboratory rats maintained there. It would thus seem as if the disease were by no means rare, and of wide geographical distribution, although no mention of it is made by Jaffé (1931). The isolation from this spontaneous rat polyarthritis of a pleuropneumonia-like organism is at the present moment of considerable interest since Swift and Brown (1939) claim to have obtained a pleuropneumonia-like organism from two cases of human rheumatism. The possible bearing of our observations on human rheumatic conditions is now being actively investigated. The fact that a spontaneous infectious polyarthritis can be studied experimentally under laboratory conditions is likely to throw further light on the human disease. In this connexion, chemotherapeutic experiments, which will shortly be published in full, are of special interest, for gold salts have long been employed empirically in the treatment of human arthritic infections and these salts appear to have a remarkable action on experimental infections with the pleuropneumonia-like organisms of mice and rats. The sulphonamide group of drugs on the other hand has no action on the polyarthritis of rats. In the pleuropneumonia-like organisms there appears to exist a group of agents many of which have a tendency to produce arthritis in various animal species.

CONCLUSION

A pleuropneumonia-like organism has been isolated in pure culture from a spontaneous polyarthritis in

the rat, and has been shown to be the causal agent of the disease.

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BACTERIOSTATIC ACTION OF SULPHANILAMIDE IN VITRO

INFLUENCE OF FRACTIONS ISOLATED FROM HÆMOLYTIC STREPTOCOCCI

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SINCE the introduction of the sulphanilamide group of drugs in the treatment of infections, their mode of action has been much discussed. There is little evidence that they act mainly by stimulating the defence mechanisms of the body (McIntosh and Whitby 1939). It seems rather that they produce their effect chiefly by direct action on the bacterial cells, possibly by preventing the development, or bringing about the destruction, of the surface immunising antigens upon which the capacity to resist the defence mechanisms of the host appears largely to depend. This suggestion is supported by the fact that the capsules of pneumococci growing in vivo in the presence of M. & B. 693 appear to undergo degeneration and in later stages are no longer demonstrable (Telling and Oliver 1938).

This phenomenon however, as McIntosh and Whitby have pointed out, may be merely part of the degenerative process accompanying death of the organisms in vivo and not necessarily due to direct action of the drug on the bacterial cell. The results of tests in vitro and in vivo indicate that the drugs do not produce their effect by simple germicidal action, since there is a short lag period before they become effective, during which the organisms may multiply at their normal rate, or there may even be an initial stimulation of growth (Colebrook, Buttle and O'Meara 1936, Finklestone-Sayliss, Paine and Patrick 1937). It seems rather that the main action of the drugs is bacteriostatic, preventing the organisms from multiplying to their normal extent, by interference with their metabolic activities. This, it is suggested, may be brought about by inactivation of certain enzyme systems responsible for the breakdown of complex proteins. Evidence in favour of this view has been brought forward by Lockwood (1938) who has shown that the inhibition of growth of hæmolytic streptococci in serum by sulphanilamide is greatly decreased if a small amount of peptone is present. He suggests that sulphanilamide prevents the organisms from breaking down the complex serum proteins, but they are still able to utilise the simpler breakdown products of protein, such as peptone, as nutritive material. Attempts to demonstrate a direct action of the drugs on the metabolic activity of certain bacteria have not yet met with success (Mellon and Bambas 1937, Barron and Jacobs 1937).

In the present paper this theory has been investigated further and attempts have been made to determine whether substances other than peptone are antibacteriostatic. In preliminary experiments, employing small inocula of a highly sulphanilamide-sensitive group C strain of hæmolytic streptococcus, it was found that in media such as heart broth or Hartley broth relatively large amounts of peptone (1 per cent. or more) were required to produce any marked antibacteriostatic effect and the same result was obtained by enriching the medium with similar amounts of glucose or serum. It was also found that the addition to the medium of relatively small amounts of heat-killed bacterial cells of the homologous strain enabled small numbers of organisms to grow in dilutions of sulphanilamide normally producing complete inhibition—an effect similar to that produced, according to Lockwood, by peptone in serum. It seemed that the two effects might be brought about in the same way—namely, by the provision of favourable nutritive material. There was a further possibility however that the killed bacterial cells might produce their effect by supplying a sufficient concentration of a necessary enzyme factor which enables the organism to overcome the inhibitory action of the sulphanilamide.

It appeared that an explanation might be forthcoming if it were found possible to isolate from the bacterial cells the substance responsible for their antibacteriostatic activity, and submit it to chemical analysis. Accordingly attempts have been made to fractionate the bacteria in various ways and to test each fraction separately for its ability to overcome the bacteriostatic action of sulphanilamide and M. & B. 693 in different media.

EXPERIMENTAL

Fractions have been obtained from two different strains of hæmolytic streptococci by methods similar to those employed in the isolation of immunising fractions from hæmolytic streptococci (Stamp and Hendry 1937), involving extraction with dilute acids and alkalis.

The method of testing for antibacteriostatic activity consisted in incorporating a standard amount of each fraction in a series of tubes of medium containing varying dilutions of sulphanilamide or M. & B. 693. Each series of tubes together with a control set containing no fraction was then inoculated with a standard number of viable organisms, incubated and observed daily for the development of turbidity. With a suitably small inoculum, a degree of turbidity equal to that of a control sulphanilamide-free culture developed in the control series in the higher dilutions of the drug, while the tubes with the lower dilutions remained permanently clear. A similar effect was obtained with sets of dilutions containing some of the fractions tested, while with other fractions maximal turbidity rapidly developed in all dilutions, indicating that the fractions possessed antibacterio-

static activity. An approximate indication as to the relative activity of different fractions has been obtained by determining the smallest amount of each required to produce maximal growth in all dilutions in a given time. Another method employed in estimating the activity of different fractions has been to carry out daily viable counts on organisms growing in the presence of the fractions in suitable concentrations of the drug. This method has of necessity been used on occasions when whole blood has constituted the test medium, but apart from such cases appears to have no advantage over the other method, besides being much more laborious.

MATERIAL AND METHODS

Strains of hæmolytic streptococci.—Strain "S.34" isolated from bovine mastitis, belonging to the sorbitol-positive, trehalose-negative subgroup of group C, has been used in the majority of tests. It has been found to be very sensitive to the action of sulphanilamide and M. & B. 693 in vitro, but is only relatively slightly affected by the drugs in vivo. Strain "Richards" isolated from puerperal septicæmia, belonging to group A, type 3, has also been employed on a number of occasions. It has been found to be less sensitive than "S.34" to the action of the drugs in vitro, though more sensitive than other group A strains tested. It is however strongly inhibited in vivo.

Size of inoculum.—Preliminary tests with each strain were carried out employing inocula of varying size, to determine the maximum number of organisms that would grow out in high dilutions of the drug in different media while remaining permanently inhibited in the lower dilutions. The most suitable inoculum of both strains for producing this effect was found to be approximately 1000 viable organisms (from an 18-hour Hartley-broth culture) in 5 c.cm. of medium. Larger inocula (100,000 organisms or more) tended to grow out in the lowest dilutions employed, though the appearance of turbidity might be delayed for 24–48 hours or longer.

Media.—Hartley broth or heart broth has been employed in nearly all experiments. Hartley broth has been prepared in the usual way by the tryptic digestion of horse muscle, and different batches have been found to possess an amino-N content of between 0·07 and 0·1 per cent. as estimated by Sörensen's method of formol titration. The inhibitory action of the drugs has been found to be fairly constant in repeated tests with the same batch of medium, but varied much more from one batch to another particularly with Hartley broth. With one or two batches of this medium it has been found impossible to obtain permanent inhibition of growth in high concentrations of the drugs, even when very small inocula were used, the organisms tending to grow out after four or five days' incubation. Excessive autoclaving in the preparation of the medium appeared to favour this effect. It did not however seem more liable to occur in batches giving particularly luxuriant growth. It was found advisable to avoid using such batches in testing different fractions, since though an indication was obtained as to relative antibacteriostatic activity, the results were not as clear-cut as when batches allowing a greater degree of inhibition of growth were used.

Whole defibrinated human and rabbit blood have also been used in some tests. With these media also it has rarely been found possible to obtain permanent inhibition of growth and in such cases reliance has been placed on the acceleration in the rate of growth produced by different fractions in estimating antibacteriostatic activity.

Preparation of sets of dilutions of the drugs.—500 mg. of sulphanilamide or M. & B. 693 has been sterilised by autoclaving and dissolved in 500 c.cm. of medium. A series of twelve dilutions from 1/1000 to 1/5,000,000 has been made up in the medium in 200 c.cm. amounts with aseptic precautions and transferred to sets of sterile $\frac{3}{4}$ in. tubes in 4·5 c.cm. quantities.

Method of testing fractions.—A standard amount of each fraction or other substance to be tested, contained in 0·5 c.cm. of saline or extract, was added to 4·5 c.cm. of each of the dilutions of drug. In addition one set of dilutions received an equal amount of saline as a control. The final dilutions of drug in each case have therefore been slightly greater than those indicated in the tables. All tubes were then inoculated with approximately 1000 organisms and after shaking were incubated at 37° C. Tubes were shaken daily and observed for the development of turbidity. In the tables which follow the results recorded on each day during the first week have been set down in separate columns (+ = the development of a degree of turbidity equal to that of a control tube containing no drug; $\pm$ = intermediate degrees of turbidity; − = no visible growth, or in tests of acid extracts a slight turbidity similar to that of uninoculated control tubes). It was found that growth rarely developed in any tube after the first week. Cultures were therefore discarded after 10–14 days' incubation.

Very occasionally contaminants developed in certain tubes. Usually they were easily recognised from their atypical growth. In doubtful cases, cultures were plated out.

METHOD OF ISOLATION OF FRACTIONS

The material for fractionation was prepared by growing strain "S.34" or strain "Richards" in 100 litres of Hartley broth for 24 hours at 37° C. The bacterial cells were allowed to sediment at 0° C., the bulk of the supernatant broth was siphoned off, and the organisms were centrifuged down. A small quantity of the supernatant broth was filtered and set aside for testing along with the fractions. The deposited cells were resuspended in 300 c.cm. of distilled water and shaken for three hours at 37° C. They were then recentrifuged and the supernatant washings were also filtered and set aside for testing. After one more washing in distilled water the cells were resuspended in 600 c.cm. of distilled water and divided into two portions. To one portion 2N HCl was added to give a final concentration of approximately N/25 HCl. To the other portion 2N NH_4OH was added to give the same concentration of NH_4OH. Each suspension was shaken at 37° C. overnight and then centrifuged until the supernatants were almost clear. They were then passed through Chamberland L3 filters and the filtrates were neutralised to pH 7·4. At this pH the HCl extract formed a dense precipitate. A part of this extract was set aside for testing and the remainder was divided into two fractions by centrifuging. The clear supernatant was removed and the precipitate redissolved in dilute acid. After one reprecipitation it was redissolved in dilute HCl and neutralised.

The filtered NH_4OH extract remained water-clear on neutralisation. A dense precipitate formed, however, on adjusting the pH to 4–5. A portion of the crude neutralised extract was set aside for testing, and the remainder fractionated by precipitation in this way. The pH4-precipitate was reprecipitated once from solution in dilute NaOH, then redissolved in dilute NaOH and neutralised. The clear supernatant at pH 4 was neutralised. All manipulations were carried out as far as possible with aseptic precautions. In the majority of fractionations no attempt was made to isolate the fractions in a solid state. A rough estimate of the total amount of dissolved organic material present in each solution was obtained by precipitating an aliquot part with 9 volumes of alcohol, drying and weighing the precipitate, and also, in some cases, by taking an aliquot part down to dryness in vacuo over phosphorus pentoxide and weighing, allowance being made for the weight of NH_4Cl calculated to be present. Each solution was then diluted with saline, so as to contain between 100–200 mg. per 100 c.cm. of dissolved organic material. The addition

TABLE I—EFFECT OF WATER-SOLUBLE, HCL-SOLUBLE AND NH_4OH-SOLUBLE FRACTIONS ON THE GROWTH OF STRAIN "S.34" IN HEART BROTH WITH VARYING CONCENTRATIONS OF SULPHANILAMIDE

Dilution of drug	Control, no extract							Filtrate of 24-hr. Hartley broth culture							Crude water-soluble fraction							Crude HCl-soluble fraction						
	1	2	3	4	5	6	7	1	2	3	4	5	6	7	1	2	3	4	5	6	7	1	2	3	4	5	6	7
1/1000	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−
1/2500	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−
1/5000	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−
1/10,000	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−
1/25,000	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−
1/50,000	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−
1/100,000	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−
1/250,000	−	−	−	−	−	−	−	−	−	+	+	+	+	+	−	−	−	+	+	+	+	−	−	+	+	+	+	+
1/500,000	−	−	−	−	−	−	−	±	±	+	+	+	+	+	±	+	+	+	+	+	+	−	−	+	+	+	+	+
1/1 × 10^6	−	−	−	−	−	−	−	±	+	+	+	+	+	+	±	+	+	+	+	+	+	−	−	+	+	+	+	+
1/2·5 × 10^6	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	±	+	+	+	+	+	+
1/5 × 10^6	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+

Dilution of drug	Crude NH_4OH-soluble fraction							Precipitate at pH 4 of crude NH_4OH-soluble fraction							Supernatant at pH 4 of crude NH_4OH-soluble fraction						
	1	2	3	4	5	6	7	1	2	3	4	5	6	7	1	2	3	4	5	6	7
1/1000	−	−	+	+	+	+	+	−	−	−	−	−	−	−	−	+	+	+	+	+	+
1/2500	−	±	+	+	+	+	+	−	−	−	−	−	−	−	−	+	+	+	+	+	+
1/5000	−	±	+	+	+	+	+	−	−	−	−	−	−	−	−	+	+	+	+	+	+
1/10,000	−	−	+	+	+	+	+	−	−	−	−	−	−	−	−	+	+	+	+	+	+
1/25,000	−	−	+	+	+	+	+	−	−	−	−	−	−	−	−	+	+	+	+	+	+
1/50,000	−	+	+	+	+	+	+	−	−	−	−	−	−	−	−	+	+	+	+	+	+
1/100,000	−	−	+	+	+	+	+	−	−	−	−	−	−	−	−	+	+	+	+	+	+
1/250,000	−	+	+	+	+	+	+	−	−	−	+	+	+	+	−	+	+	+	+	+	+
1/500,000	−	+	+	+	+	+	+	±	+	+	+	+	+	+	−	+	+	+	+	+	+
1/1 × 10^6	−	+	+	+	+	+	+	±	+	+	+	+	+	+	−	+	+	+	+	+	+
1/2·5 × 10^6	±	+	+	+	+	+	+	+	+	+	+	+	+	+	±	+	+	+	+	+	+
1/5 × 10^6	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+

Tubes observed daily during the first week for visible signs of growth and the results recorded in columns 1–7.

+ = growth complete
± = intermediate degrees of turbidity
− = no visible growth

of 0·5 c.cm. quantities of these solutions to 4·5 c.cm. of medium resulted in a final concentration of 10–20 mg. per 100 c.cm.

ANTIBACTERIOSTATIC ACTIVITY OF DIFFERENT FRACTIONS

An investigation has been carried out of the effect of these fractions isolated from strain "S.34" on the inhibition of growth of the homologous strain in heart broth containing sulphanilamide, and the results are shown in table I.

It will be seen that the crude NH_4OH extract exerted a marked antibacteriostatic effect on sulphanilamide, growth being complete in all dilutions of the drug after 72 hours. A similar effect was obtained with the pH4-supernatant fraction of the NH_4OH extract. None of the other fractions have produced a result appreciably different from that of the control and have failed to support growth in all dilutions below 1/250,000. Control tests showed that the effect obtained was not due to the presence of NH_4Cl in the active extract. It appeared therefore that a substance capable of neutralising the inhibitory action of sulphanilamide in vitro might be isolated from the bacterial cells by extraction with NH_4OH, but not with dilute HCl. This substance was not present in an appreciable amount in a filtrate of the culture nor in an aqueous extract, and was not precipitated from the NH_4OH extract at pH 4. Essentially similar results have been obtained with

TABLE II—EFFECT OF HCL-SOLUBLE AND NH_4OH-SOLUBLE FRACTIONS ON THE GROWTH OF STRAIN "S.34" IN HARTLEY BROTH WITH VARYING CONCENTRATIONS OF SULPHANILAMIDE

Dilution of drug	Control, no extract							Crude NH_4OH-soluble fraction							Crude NH_4OH-soluble fraction, N/10 HCl treated							Crude HCl-soluble fraction						
	1	2	3	4	5	6	7	1	2	3	4	5	6	7	1	2	3	4	5	6	7	1	2	3	4	5	6	7
1/1000	−	−	−	−	−	−	−	±	+	+	+	+	+	+	−	±	+	+	+	+	+	−	−	−	−	−	−	−
1/2500	−	−	−	−	−	−	−	±	+	+	+	+	+	+	−	±	+	+	+	+	+	−	−	−	−	−	−	−
1/5000	−	−	−	−	−	−	−	±	+	+	+	+	+	+	−	±	+	+	+	+	+	−	−	−	−	−	−	−
1/10,000	−	−	−	−	−	−	−	±	+	+	+	+	+	+	−	±	+	+	+	+	+	−	−	−	−	−	−	−
1/25,000	−	−	−	−	−	−	−	±	+	+	+	+	+	+	−	±	+	+	+	+	+	−	−	−	−	−	−	−
1/50,000	−	−	−	−	−	−	−	±	+	+	+	+	+	+	−	±	+	+	+	+	+	−	−	−	−	−	−	−
1/100,000	−	−	−	−	−	−	−	±	+	+	+	+	+	+	−	±	+	+	+	+	+	−	−	−	−	−	−	−
1/250,000	−	−	−	−	−	−	−	±	+	+	+	+	+	+	−	±	+	+	+	+	+	−	−	−	−	−	−	−
1/500,000	−	−	+	+	+	+	+	+	+	+	+	+	+	+	±	+	+	+	+	+	+	−	−	−	+	+	+	+

Dilution of drug	Precipitate at pH 4 of NH_4OH-soluble fraction 10–20 mg.*							Supernatant at pH 4 of NH_4OH-soluble fraction 10–20 mg.*							Supernatant fraction 1–2 mg.*							Supernatant fraction 0·1–0·2 mg.*						
	1	2	3	4	5	6	7	1	2	3	4	5	6	7	1	2	3	4	5	6	7	1	2	3	4	5	6	7
1/1000	−	−	−	−	−	−	−	−	±	+	+	+	+	+	−	−	−	−	−	−	−	−	−	−	−	−	−	−
1/2500	−	−	−	−	−	−	−	−	+	+	+	+	+	+	−	±	+	+	+	+	+	−	−	−	−	−	−	−
1/5000	−	−	−	−	−	−	−	−	+	+	+	+	+	+	−	±	+	+	+	+	+	−	−	−	−	−	−	−
1/10,000	−	−	−	−	−	−	−	−	+	+	+	+	+	+	−	±	+	+	+	+	+	−	−	−	−	−	−	−
1/25,000	−	−	−	−	−	−	−	−	+	+	+	+	+	+	−	−	−	+	+	+	+	−	−	−	−	−	−	−
1/50,000	−	−	−	−	−	−	−	−	+	+	+	+	+	+	−	±	+	+	+	+	+	−	−	−	−	−	−	−
1/100,000	−	−	−	−	−	−	−	−	+	+	+	+	+	+	−	+	+	+	+	+	+	−	−	−	−	−	−	−
1/250,000	−	−	−	−	−	−	+	−	+	+	+	+	+	+	−	+	+	+	+	+	+	−	−	−	−	−	−	−
1/500,000	−	±	+	+	+	+	+	±	+	+	+	+	+	+	−	+	+	+	+	+	+	−	−	+	+	+	+	+

* mg. per 100 c.cm.

TABLE III—EFFECT OF THE NH_4OH-SOLUBLE pH4-SUPERNATANT FRACTION OF "S.34," UNHEATED AND HEATED AT 100° C. FOR 10 MINUTES AND IN DIFFERENT CONCENTRATIONS, ON THE BACTERIOSTATIC ACTION OF SULPHANILAMIDE IN HARTLEY BROTH

Dilution of drug	Control, no extract							NH_4OH-soluble pH4-soluble fraction, unheated, 10–20 mg.*							Unheated fraction 1–2 mg.*							Heated fraction 1–2 mg.*						
	1	2	3	4	5	6	7	1	2	3	4	5	6	7	1	2	3	4	5	6	7	1	2	3	4	5	6	7
1/1000	−	−	−	−	−	−	−	±	+	+	+	+	+	+	−	+	+	+	+	+	+	−	±	+	+	+	+	+
1/2500	−	−	−	−	−	−	−	±	+	+	+	+	+	+	−	+	+	+	+	+	+	−	+	+	+	+	+	+
1/5000	−	−	−	−	+	+	+	±	+	+	+	+	+	+	−	+	+	+	+	+	+	−	+	+	+	+	+	+
1/10,000	−	−	−	−	+	+	+	±	+	+	+	+	+	+	−	+	+	+	+	+	+	−	+	+	+	+	+	+
1/25,000	−	−	−	−	−	−	−	±	+	+	+	+	+	+	−	+	+	+	+	+	+	−	+	+	+	+	+	+
1/50,000	−	−	−	−	−	−	−	±	+	+	+	+	+	+	−	+	+	+	+	+	+	−	+	+	+	+	+	+
1/100,000	−	−	−	−	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	−	+	+	+	+	+	+
1/250,000	−	−	±	+	+	+	+	+	+	+	+	+	+	+	±	+	+	+	+	+	+	−	+	+	+	+	+	+
1/500,000	±	+	+	+	+	+	+	+	+	+	+	+	+	+	±	+	+	+	+	+	+	±	+	+	+	+	+	+
	Unheated fraction 0·1–0·2 mg.*							Heated fraction 0·1–0·2 mg.*							Unheated fraction 0·01–0·02 mg.*							Heated fraction 0·01–0·02 mg.*						
	1	2	3	4	5	6	7	1	2	3	4	5	6	7	1	2	3	4	5	6	7	1	2	3	4	5	6	7
1/1000	−	−	−	+	+	+	+	−	−	−	+	+	+	+	−	−	−	−	−	+	+	−	−	−	±	+	+	+
1/2500	−	−	−	+	+	+	+	−	−	±	+	+	+	+	−	−	−	−	−	+	+	−	−	−	±	+	+	+
1/5000	−	−	±	+	+	+	+	−	−	±	+	+	+	+	−	−	−	+	+	+	+	−	−	−	−	+	+	+
1/10,000	−	−	+	+	+	+	+	−	−	±	+	+	+	+	−	−	−	±	+	+	+	−	−	−	+	+	+	+
1/25,000	−	−	−	+	+	+	+	−	−	±	+	+	+	+	−	−	−	−	+	+	+	−	−	−	±	+	+	+
1/50,000	−	−	+	+	+	+	+	−	−	±	+	+	+	+	−	−	−	±	+	+	+	−	−	−	−	+	+	+
1/100,000	−	−	+	+	+	+	+	−	−	+	+	+	+	+	−	−	−	+	+	+	+	−	−	−	±	+	+	+
1/250,000	−	−	+	+	+	+	+	−	−	+	+	+	+	+	−	−	−	+	+	+	+	−	−	+	+	+	+	+
1/500,000	±	+	+	+	+	+	+	±	+	+	+	+	+	+	±	+	+	+	+	+	+	−	±	+	+	+	+	+

* mg. per 100 c.cm.

the active NH_4OH-soluble fractions in Hartley broth containing varying dilutions of M. & B. 693.

It was of interest to determine the concentration of the active fraction necessary to produce any effect and also whether it was possible to inactivate it by treatment with dilute HCl in order to account for the lack of activity of the HCl extract. Another fractionation has therefore been carried out in the same way. A portion of the crude NH_4OH-soluble fraction was acidified to a concentration of N/10 HCl, allowed to stand overnight at 37° C., and then neutralised. This was tested in Hartley broth along with the other fractions including varying concentrations of the NH_4OH-soluble pH4-supernatant fraction. The batch of Hartley broth employed in this test permitted no growth of the standard inoculum in concentrations of the drug below 1/500,000. The results of this experiment are shown in table II. It will be seen that the results obtained in the previous test have been confirmed. There is no indication that the activity of the crude NH_4OH extract was destroyed by treatment with N/10 HCl. Further tests have confirmed this finding. It seems likely therefore that the inactivity of the HCl extract is due to the fact that the active substance cannot be extracted from the bacterial cells by dilute acid. The NH_4OH-soluble pH4-supernatant fraction is shown to be active in this batch of medium in a concentration of 1–2 mg. per 100 c.cm., but produces no appreciable effect in a concentration of 0·1–0·2 mg.

Varying concentrations of this active fraction have been tested in another batch of Hartley broth in which the inhibitory action of sulphanilamide was not as marked. The effect of heat on the activity of the fraction has also been investigated by testing varying concentrations of the fraction previously heated at 100° C. for ten minutes. The results are shown in table III.

It will be seen that in this batch of medium a concentration of the fraction as low as 0·01–0·02 mg. per 100 c.cm. had an appreciable anti-inhibitory effect. In this concentration, turbidity developed in all dilutions of the drug by the sixth day, while in the control series growth was permanently inhibited

TABLE IV—EFFECT OF DIFFERENT FRACTIONS ISOLATED FROM STRAIN "RICHARDS" ON THE BACTERIOSTATIC ACTION OF SULPHANILAMIDE IN HARTLEY BROTH

Dilution of drug	Control, no extract							Crude water-soluble fraction							Crude HCl-soluble fraction						
	1	2	3	4	5	6	7	1	2	3	4	5	6	7	1	2	3	4	5	6	7
1/1000	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−
1/2500	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−
1/5000	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	+	+	+	+	+	+
1/10,000	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−
1/25,000	−	−	−	−	−	−	−	−	+	+	+	+	+	+	−	−	−	−	−	−	−
1/50,000	±	+	+	+	+	+	+	±	+	+	+	+	+	+	−	−	−	−	−	+	+
1/100,000	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
	Crude NH_4OH-soluble fraction							Precipitate at pH 4 of NH_4OH-soluble fraction							Supernatant at pH 4 of NH_4OH-soluble fraction						
	1	2	3	4	5	6	7	1	2	3	4	5	6	7	1	2	3	4	5	6	7
1/1000	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	±	+	+	+	+	+
1/2500	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	±	+	+	+	+	+
1/5000	±	+	+	+	+	+	+	−	−	−	−	−	−	−	−	±	+	+	+	+	+
1/10,000	±	+	+	+	+	+	+	−	−	−	−	−	−	−	−	−	−	+	+	+	+
1/25,000	±	+	+	+	+	+	+	−	−	−	−	−	−	−	−	±	+	+	+	+	+
1/50,000	−	−	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+
1/100,000	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+

TABLE V—EFFECT OF THE NH_4OH-SOLUBLE pH4-SUPERNATANT FRACTIONS ISOLATED FROM "RICHARDS" AND "S.34" STRAINS ON THE GROWTH OF THESE ORGANISMS IN HARTLEY BROTH WITH VARYING CONCENTRATIONS OF SULPHANILAMIDE

Dilution of drug	Inoculated with—	Control, no extract							Fraction isolated from "Richards"							Fraction isolated from "S.34"						
		1	2	3	4	5	6	7	1	2	3	4	5	6	7	1	2	3	4	5	6	7
1/1000	"Richards"	−	−	−	−	−	−	−	−	±	+	+	+	+	+	±	+	+	+	+	+	+
1/2500		−	−	−	−	−	−	−	−	±	+	+	+	+	+	±	+	+	+	+	+	+
1/5000		−	−	−	−	−	−	−	−	±	+	+	+	+	+	±	+	+	+	+	+	+
1/10,000		−	−	−	−	−	−	−	−	−	+	+	+	+	+	±	+	+	+	+	+	+
1/25,000		−	−	−	−	−	−	−	−	±	+	+	+	+	+	+	+	+	+	+	+	+
1/50,000		±	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+
1/100,000		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
1/250,000		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
1/500,000		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
1/1 × 10^6		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
1/1000	"S.34"	−	−	−	−	−	−	−	±	+	+	+	+	+	+	+	±	+	+	+	+	+	+
1/2500		−	−	−	−	−	−	−	±	+	+	+	+	+	+	+	±	+	+	+	+	+	+
1/5000		−	−	−	−	−	−	−	±	+	+	+	+	+	+	+	±	+	+	+	+	+	+
1/10,000		−	−	−	−	−	−	−	±	+	+	+	+	+	+	+	±	+	+	+	+	+	+
1/25,000		−	−	−	−	−	−	−	+	+	+	+	+	+	+	+	±	+	+	+	+	+	+
1/50,000		±	+	+	+	+	+	+	+	+	+	+	+	+	+	+	±	+	+	+	+	+	+
1/100,000		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
1/250,000		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
1/500,000		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
1/1 × 10^6		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+

in several of the higher concentrations. Furthermore the activity of the fraction was not appreciably affected by heating, the heated and unheated fractions producing very similar results in all concentrations employed.

Fractions have also been isolated from strain "Richards" in the way already described and tested in Hartley broth with varying concentrations of sulphanilamide. The results shown in table IV indicate that an active fraction similar to that obtained from "S.34" may be isolated from this strain also. It was of interest to determine whether these fractions were capable of stimulating the growth in sulphanilamide of the heterologous as well as the homologous strain. Accordingly the activity of both NH_4OH-soluble pH4-supernatant fractions was tested with each strain. The results shown in table V indicate that the action of the fraction is non-specific, the growth of the homologous and heterologous strains being promoted to a similar extent by each fraction. Tests of the "Richards" active fraction were also carried out in heart broth, but gave less consistent results. In certain batches of this medium a higher concentration of the active fractions than that normally employed appears to be required to produce an appreciable antibacteriostatic effect.

FRACTIONATION OF THE NH_4OH-SOLUBLE pH4-SUPERNATANT FRACTION OF "S.34"

An attempt was made to fractionate the active fraction further and to isolate it in a solid state.

The washed bacterial cells from 120 litres of Hartley broth culture of "S.34" were repeatedly extracted overnight at 37° C. with N/25 NH_4OH. The first two extracts containing the great bulk of extractable material were centrifuged, pooled and adjusted to pH 4. The pH4-precipitate, together with a residue of bacterial cells, was centrifuged down, leaving 900 c.cm. of clear supernatant. This filtered with ease through an L3 candle and was neutralised. To 600 c.cm. of the filtrate was added 1200 c.cm. of absolute alcohol. After standing overnight at 0° C., the precipitate which formed was centrifuged down, washed with absolute alcohol and ether and dried in vacuo over phosphorus pentoxide. The yield of this "67 P" fraction was approximately 2 per cent. of the whole NH_4OH-soluble pH4-supernatant fraction. It appeared to consist mainly of material similar to the pH4-precipitate fraction.

To the supernatant with two volumes of alcohol a further seven volumes or 4200 c.cm. of absolute

TABLE VI—EFFECT OF DIFFERENT FRACTIONS ISOLATED FROM THE NH_4OH-SOLUBLE pH4-SUPERNATANT FRACTION OF "S.34," AND ALSO OF PEPTONE AND GLUCOSE ON THE BACTERIOSTATIC ACTIVITY OF SULPHANILAMIDE IN HARTLEY BROTH

Dilution of drug	Control, no fraction							Peptone 100 mg.*							Glucose 100 mg.*						
	1	2	3	4	5	6	7	1	2	3	4	5	6	7	1	2	3	4	5	6	7
1/1000	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−
1/2500	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−
1/5000	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−
1/10,000	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−
1/25,000	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−
1/50,000	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−
1/100,000	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−
1/250,000	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−
	Fraction "67 P" 10 mg.*							Fraction "90 P" 10 mg.*							Fraction "90 S" 10 mg.*						
	1	2	3	4	5	6	7	1	2	3	4	5	6	7	1	2	3	4	5	6	7
1/1000	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	+	+	+	+
1/2500	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	±	+	+	+	+	+
1/5000	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	±	+	+	+	+	+
1/10,000	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	±	+	+	+	+	+
1/25,000	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	±	+	+	+	+	+
1/50,000	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	±	+	+	+	+	+
1/100,000	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	+	+	+	+	+	+
1/250,000	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	+	+	+	+	+	+

* mg. per 100 c.cm.

alcohol were added. After standing overnight at 0° C., the precipitate which formed was centrifuged down, washed and dried off as before. The yield of this "90 P" fraction was found to be approximately 20 per cent. of the total. The supernatant with nine volumes of alcohol was then taken down to dryness in vacuo and drying was completed over P_2O_5 (phosphorus pentoxide). This "90 S" fraction was found to contain approximately one-quarter of its weight of NH_4Cl. The total concentration of dissolved material other than NH_4Cl present in the pH4-supernatant fraction of the NH_4OH extract was approximately 600 mg. per 100 c.cm. This represents a yield of between 5–10 per cent. of the total weight of the unfractionated cells, as compared with a yield of 10–20 per cent. of the pH4-precipitate fraction. These yields are however only approximate and appear to vary considerably with different batches of cells.

The three fractions—"67 P," "90 P," and "90 S"—isolated from the crude NH_4OH-soluble pH4-supernatant fraction have been tested for antisulphanilamide activity in Hartley broth in the usual way, in a concentration of 10 mg. per 100 c.cm., the solutions of the fractions being heated to 100° C. for ten minutes to sterilise before incorporating in the medium. Tests of peptone and glucose added to the medium in ten times this concentration have also been included in this experiment. The results are shown in table VI.

It will be seen that in this batch of medium sulphanilamide had a very marked inhibitory effect, the standard inoculum of approximately 1000 organisms failing to grow out in any of the dilutions employed in the control series. A similar effect was obtained in all the other sets of dilutions except the series containing the "90 S" fraction. This fraction appears to be strongly antibacteriostatic and allowed the organisms to grow out by the fourth day in all dilutions of the drug.

INFLUENCE OF PEPTONE AND OF "S.34" FRACTIONS ON GROWTH OF "RICHARDS" IN WHOLE BLOOD CONTAINING M. & B. 693

Experiments have been carried out to determine whether the fraction "90 S" is capable of antagonising the effect of the drugs in whole blood as well as in broth media. Tests with both "Richards" and "S.34" strains have shown that even when very small inocula consisting of approximately 10 organisms were employed in rabbit or human defibrinated blood containing either drug in a concentration of 1/5000, the organism nearly always grew out after a lag period of a few days. An indication as to the activity of different fractions under these conditions has been obtained by determining the degree to which the fractions were capable of reducing this lag period. Different fractions in varying concentrations contained in 0·5 c.cm. of saline have been added to 4·5 c.cm. quantities of human defibrinated blood containing M. & B. 693 in a concentration of 1/10,000, and these have been inoculated with approximately 10 organisms. Cultures containing peptone and controls consisting only of blood with and without the drug were also included in the test. The rate of growth in each culture was estimated by daily viable counts, the rapid viable counting method described by Miles and Misra (1938) being employed, and the results are shown in fig. 1. It will be seen that in this test the fraction "90 S" produced an appreciable acceleration in the rate of growth of the organisms in a concentration as low as 1/1,000,000. A similar effect was produced by peptone but only when considerably larger amounts were present. The acid extract, as on previous occasions, was completely inactive. The results therefore with whole blood, though not as clear-cut as in the previous experiment with Hartley broth, tend to confirm the view that fraction "90 S" contains the active factor.

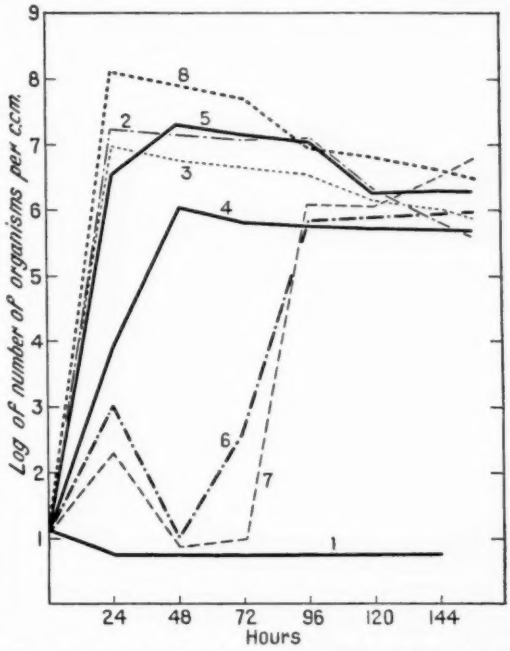

FIG. 1—Showing the effect of different fractions isolated from streptococcus strain "S.34," and also of peptone, on the growth of strain "Richards" in defibrinated human blood containing M. & B. 693 in a concentration of 1 in 10,000.

1 = Crude HCl-soluble fraction (10 mg. per 100 c.cm.)
2 = Fraction "90 S" .. .. (10 ,, ,, ,, ,,)
3 = ,, ,, ... (1 ,, ,, ,, ,,)
4 = ,, ,, ... (0·1 ,, ,, ,, ,,)
5 = Peptone .. .. .. (100 ,, ,, ,, ,,)
6 = ,, ... (10 ,, ,, ,, ,,)
7 = Control. No fraction.
8 = ,, ,, No M. & B. 693.

THE CHEMICAL PROPERTIES OF FRACTION "90 S"

By D. BEALL, Ph.D.

This fraction is a hygroscopic, amorphous yellow powder completely soluble in water. After drying in vacuo nitrogen determinations were made by nesslerisation before and after Kjeldahl digestion, thus giving the ammonia nitrogen and total nitrogen of the samples. The free amino-acid content was determined by the colorimetric method of Folin. Owing to the complexity of the mixture no attempt was made to obtain C. and H. figures, but the ash content was estimated. The amount of reducing sugar before and after acid hydrolysis was also found. The figures obtained are given in table VII together with "corrected values" on the assumption that all the ammonia nitrogen was present as ammonium chloride and also corrected for an ammonium chloride-ash free basis.

The combined reducing sugar was estimated by refluxing 28–36 mg. samples for one hour with 5 c.cm. N. HCl, exactly neutralising the excess acid with N.NaOH and determining the liberated sugar by the Harding modification of the Schafer-Hartmann method.

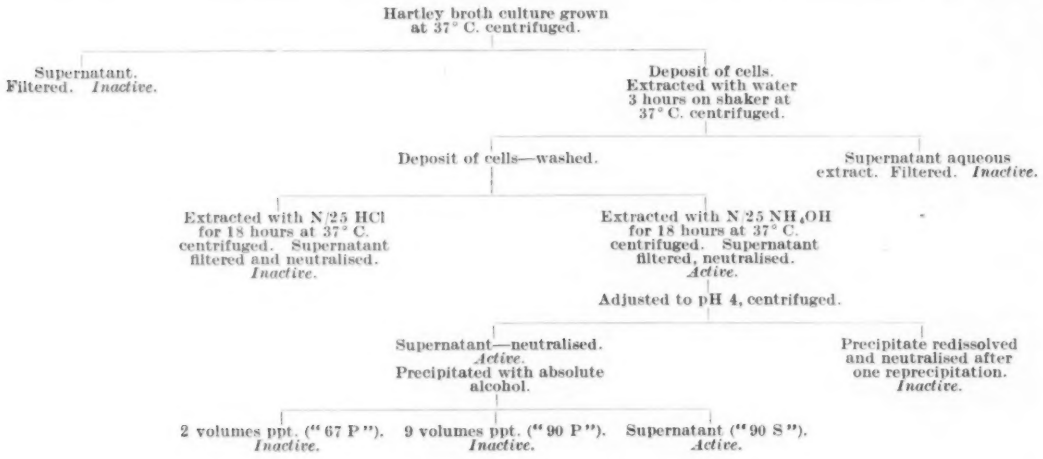
Hartley broth culture grown at 37° C. centrifuged.
Supernatant. Filtered. Inactive.
Deposit of cells. Extracted with water 3 hours on shaker at 37° C. centrifuged.
Deposit of cells—washed.
Supernatant aqueous extract. Filtered. Inactive.
Extracted with N/25 HCl for 18 hours at 37° C. centrifuged. Supernatant filtered and neutralised. Inactive.
Extracted with N/25 NH4OH for 18 hours at 37° C. centrifuged. Supernatant filtered, neutralised. Active.
Adjusted to pH 4, centrifuged.
Supernatant—neutralised. Active. Precipitated with absolute alcohol.
Precipitate redissolved and neutralised after one reprecipitation. Inactive.
2 volumes ppt. ("67 P"). Inactive.
9 volumes ppt. ("90 P"). Inactive.
Supernatant ("90 S"). Active.

FIG. 2—Method of isolation of fractions

In order to obtain further information about the form of the combined nitrogen, a number of qualitative tests were carried out using a 1 per cent. solution of the crude material. It gave a positive xanthoproteic reaction and a very strong ninhydrin reaction. The modified Millon reaction (mercuric-nitrite test) and formaldehyde tryptophane reactions were negative. A negative biuret reaction was obtained even after allowing an N.NaOH solution to stand for 48 hours in a desiccator over sulphuric acid in order to remove the ammonia. No precipitation occurred with trichloracetic acid, tannic acid, or sulphosalicylic acid. The Molisch reaction was positive.

TABLE VII—ANALYSIS OF FRACTION "90 S"

—	Crude material (per cent.)	Calculated values	
		NH_4Cl-free basis	NH_4Cl-ash free basis
Ammonia N	7·1 (27·2 % NH_4Cl)	—	—
Total N ..	16·1	12·4	14·3
Amino-acid N ..	7·6	10·4	12·1
Ash	9·9	13·6	—
Free reducing sugar..	0	0	0
Reducing sugar after hydrolysis.. ..	5·8	8·0	9·2

DISCUSSION

The results of experiments recorded in this paper indicate that it is possible to isolate from broth cultures of hæmolytic streptococci a substance capable of antagonising the bacteriostatic action of sulphanilamide and M. & B. 693 in different media. The substance may be extracted from the bacterial cells by means of dilute NH_4OH, but is not removed in appreciable amounts by extraction with water or dilute HCl. It is not precipitated from the ammoniacal extract on acidifying to a pH of 4–5, nor by the addition of nine volumes of alcohol (fig. 2). The activity of the substance is not affected by heating to 100° C. and does not appear to be highly specific since it produces a growth-promoting effect in the presence of the drugs not only on the homologous strain but also on a strain belonging to a different serological group. The substance is active in low concentrations, under favourable conditions exerting an appreciable effect in a dilution of 1 in a million, while a very marked effect has been obtained in nearly all experiments in a concentration of 1/10,000. A preliminary chemical analysis of the partially purified active substance indicates that it consists of material of relatively low molecular weight. It gives negative tests with various protein precipitants and also a negative biuret reaction. A positive Molisch reaction and also estimations of the amount of reducing substance on hydrolysis show the presence of a small amount of carbohydrate material. A strongly positive ninhydrin reaction was obtained indicating the presence of free amino-acids. The fraction also contains some 10 per cent. of ash and about 25 per cent. of NH_4Cl. It is evident that further purification and analysis of the active substance must be carried out before any definite indication can be obtained as to its real chemical nature and the way it produces its antibacteriostatic effect.

There appear however to be several possible explanations of the results obtained in the present experiments, consistent with the view that the drugs exert an inhibitory influence on the activity of certain enzymes concerned in bacterial metabolism.

In the first place the active fraction may contain a necessary nutritive factor, possibly an essential amino-acid, the production of which is interfered with by the action of the drugs. This substance is unlikely to be one of the common simple amino-acids since a marked bacteriostatic effect can be obtained in a medium such as Hartley broth which contains a high concentration of these substances. But it may be one of the rarer amino-acids which the organisms have to synthesise or even consist of a more complex molecule necessary for the synthesis of bacterial protein.

There is the further possibility that the active substance is an essential part of the enzyme system affected by the drugs. It is unlikely that the activity of the fraction is due to the presence of the enzyme itself, since it is not affected by heating to 100° C. nor by treatment with dilute acids and alkalis. It may be however that the activity of the drugs is

directed not against an actual enzyme but rather against a substance of the nature of a coenzyme upon the presence of which in many cases the activity of enzymes has been shown to be entirely dependent. These substances are often relatively simple compounds of low molecular weight and are not infrequently resistant to treatment with heat, acids and alkalis. The presence of such a substance in the active fraction might therefore be responsible for the effects produced. It seems probable that the correct explanation of the antibacteriostatic activity of the fraction is to be found along these lines, but until further knowledge has been gained as to the chemical nature of the active factor it is impossible to give a definite answer to the problem.

SUMMARY

1. A fraction capable of antagonising the bacteriostatic action of sulphanilamide and M. & B. 693 in vitro has been isolated from a broth culture of a group C hæmolytic streptococcus.

2. The fraction can be extracted from the bacterial cells by means of dilute NH_4OH but not with water or dilute HCl.

3. The fraction is active in low concentrations and is resistant to heat, dilute acids and alkalis. It appears to be non-specific in its action.

4. Preliminary chemical analysis indicates that the active fraction is free from protein and consists of a mixture of substances of relatively low molecular weight, including free amino-acids.

5. An apparently similar fraction has also been isolated from a culture of a group A hæmolytic streptococcus.

6. Possible ways in which this substance may produce its antibacteriostatic effect are discussed.

I am greatly indebted to Dr. D. Beall who has very kindly carried out the chemical analysis on fraction "90 S." My thanks are also due to Mr. F. W. Jelks for his invaluable technical assistance. The general expenses connected with this investigation have been met by a specific grant from the Pilgrim Trust.

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DISTURBANCE OF MEMORY AFTER CONVULSION TREATMENT

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THE object of this paper is to report certain undesirable effects which have been noted after the administration of convulsants for the treatment of mental illness. These effects may be described as "intellectual impairment," and were observed typically as defects in memory.

The case material consists of a series of patients treated in the wards of the Maudsley Hospital during the six months March to August, 1938; most of these recovered and have been followed up to the present time. The total number of cases treated during this period by the administration of the convulsants Cardiazol or Triazol was 37, but an accurate statistical survey of all these is unfortunately impossible, owing to the elimination of over half the number: 6 patients left hospital after less than five injections; 6 patients did not improve or got clinically worse under treatment; and 9 patients were discharged without investigation of their intellectual capabilities by the detailed methods presently to be mentioned. The remaining 16 patients, most of whom have been under the personal care of one of us (G. T.), formed the basis of the present investigation. Of these, 12 were diagnosed as schizophrenic, and all but 1, who is still in hospital, improved sufficiently to return to work or household duties. Of the remaining 4 patients, 3 were suffering from depression of over eight months' duration, and 1 was in a severe obsessional state. Of the depressives, 2 made considerable improvement and left hospital; 1 is still in hospital, complaining mainly of the memory defect to be discussed; and the obsessional is still attending in the outpatient department, only slightly improved. Table I gives a summary of the cases, diagnosis, treatment, and also results of the psychological investigation which is described in the latter part of the paper.

TABLE I—SUMMARY OF CASES, TREATMENT, RESULTS AND MEMORY IMPAIRMENT

Case	Age	Diagnosis	Fits	Convulsant used	Average amount used (g.)	Result	Memory loss (noted)	Memory loss (tested)	Followed up
1	51	Dep.	13	C	0·75	Rec.	+ + +	+ + +	0
2	40	Schiz.	13	C	0·62	Rec.	+ + +	+ + +	+
3	39	Dep.	19	C	0·74	I.P.	+ + + +	+ + +	+ + +
4	36	Schiz.	12	C	0·73	Rec.	0	+ + + +	N.T.
5	35	Schiz.	8	T	0·5	Rec.	+ + + +	N.T.	Better
6	35	Obses.	7	C+I	1·0	Imp.	+ + + +	0	N.T.
7	35	Schiz.	12	C	0·73	Rec.	0	N.T.	N.T.
8	34	Dep.	13	C+T	0·66	Rec.	0	0	N.T.
9	33	Schiz.	15	C+I	0·72	Rec.	0	N.T.	N.T.
10	32	Schiz.	13	C	1·2	Rec.	+ + +	+	+ +
11	32	Schiz.	15	C	0·7	I.P.	+	+ +	+
12	30	Schiz.	13	C	0·82	Rec.	+ + +	+ + + +	+ + + +
13	29	Schiz.	13	C	0·66	Rec.	+ + +	N.T.	N.T.
14	23	Schiz.	15	C+T	2·0	Rec.	0	+ + +	N.T.
15	21	Schiz.	8	C+I	1·3	Rec.	0	N.T.	N.T.
16	16	Schiz.	5	C	1·3	Rec.	0	0	N.T.

For purposes of comparison, the doses of triazol have been given in terms of the equivalent quantity of cardiazol, 0·01 g. triazol being taken as equal to 0·5 g. cardiazol. C, cardiazol; T, triazol; I, insulin; Dep., depressive; Schiz., schizophrenic; Obses., obsessional; Rec., recovered; I.P., inpatient at present; Imp., improved. + + + +, certain impairment; + + +, almost certain impairment; + +, probable impairment; +, possible impairment; 0, no impairment; N.T., not tested.

CASES ILLUSTRATING MEMORY LOSS

It will be seen from the table that of the 16 patients, 9 complained of memory difficulty. The most striking

confirmation of this has come from the friends and relatives of the patients; in fact, attention was first drawn to the subject by the relatives of the second patient to be treated in hospital (no. 10, table I).

This patient developed an acute paranoid reaction, which progressed in hospital to a mixed schizophrenic state with catatonic features and a most florid symptomatology. After four weeks of treatment, consisting of ten convulsions, he lost most of his symptoms, and was able to go home for the weekend. There, according to his fiancée, he showed improvement, but seemed absent-minded, and had difficulty in recalling relatively unimportant matters connected with his daily life. Attention was first drawn to this deficiency on the second day, when, during conversation with some friends, he was unable to remember the name of the seaside resort where they had spent the previous afternoon. Questioning of the patient by his friends had revealed a number of other facts that he had forgotten, for instance, the name of the restaurant where they had lunched and what he had eaten; these facts were easily recalled once they had been mentioned. When last seen, eight months after treatment, he stated that it was still difficult to recall the names of people whom he had previously known quite well.

This patient also showed "lacunar amnesia," amounting to a retrograde amnesia, which covered the six weeks during which he had been most acutely ill, and the cardiazol injections had been started. This condition, which persisted for about three weeks, cleared up suddenly in three days. The amnesia can hardly be attributed to the treatment for the patient recovered from it in the course of treatment. Further, it was easily explicable on psychological grounds, as it was present at a stage of recovery when such unpleasant memories might well be suppressed.

Another case illustrating this memory difficulty is no. 5 in table I, a German refugee highly trained as a statistician and shorthand-typist. She had made a suicidal attempt during an acute paranoid psychosis, and when admitted to hospital was in a catatonic stupor. After eight convulsions induced with triazol, she made an apparently complete recovery from her attack, but started at once to complain that her memory, which had previously been exceptionally good, now played her tricks; on one occasion she was embarrassed by not being able to recall the name of a cousin whom she knew well, and who visited her in hospital. During the year preceding her illness she had learned English shorthand well enough to enable her to obtain a responsible secretarial post in this country. On recovery from her psychosis, five months after the onset, she had great difficulty in remembering this more recently acquired attainment. It had not, however, been completely forgotten, the defect involving only a certain number of signs which she had to relearn from the manual. In addition she showed some failure of retention: when she played tennis she could not retain the score during the game. This patient was discharged from hospital ten weeks after the last injection and has been interviewed three times in the six months since then. During this period, with characteristic German thoroughness, she retrained her memory by an elaborate system of self-imposed tasks, such as memorising and tabulating the contents of the shop windows of the town in which she was staying. When last seen she had obtained another position, and said that her memory gave her no more trouble. Owing to her imperfect knowledge of English it was unfortunately impossible to assess the results of the standardised tests employing vocabulary on this patient.

Another patient (no. 12, table I) came to the hospital for treatment of a rather insidious schizophrenia, which would ordinarily have been given a poor prognosis. Treated with cardiazol, she had thirteen convulsions, and made considerable clinical improvement, but insisted on leaving rather than submit to further treatment. She has since been seen in the outpatient department. At the first visit, and subsequently, her husband complained more of her forgetfulness and impaired efficiency as a housewife than of her persisting psychotic symptoms, to which he was more accustomed. Before her illness this patient had been an obsessionally efficient housewife, but now she was always forgetting where she had put things, and complaining that she could not recall names and addresses of people whom she knew quite well. Over a period of eight months since ceasing treatment her memory has improved both subjectively and objectively, but when last seen she said that she still had to use a list when shopping, as she could not yet rely on her memory.

Finally, no. 2 in table I is worthy of special note. This patient was admitted to hospital in what appeared to be a depressive state with obsessional features. During a period of two months under observation the purely affective side of her illness was to a large extent replaced by anxiety, and there were bizarre and fantastic delusions with auditory hallucinations. In fact, the patient's condition at this time would qualify her for inclusion in the ill-defined group of "depressive states with schizophrenic features." Before the onset of her illness she had been a successful business woman; there had been no complaint of defective memory on admission, nor was this demonstrated in formal testing. Since the condition appeared to be stationary it was decided to use cardiazol; she was given thirteen convulsions and showed a fair degree of improvement. This patient, towards the end of her course of treatment (which she disliked intensely), had several episodes of acute excitement which came on twelve to twenty-four hours after the convulsion and which lasted from six to eight hours; during this time she was muddled and disorientated, and would do odd things, such as polishing the furniture with metal polish. After recovery from each attack she would profess complete amnesia for the whole episode. The treatment was finally discontinued at the patient's request, and she started almost at once to complain of memory difficulties. Since these were, at first, mainly concerned with hospital matters, such as the names of patients and nurses, no great attention was paid to them. However, after her clinical state had almost returned to normal she found, when she was trying to pick up the threads of her business, that the names of customers and telephone numbers, which she had carried in her head for years, now eluded her. Seen in the outpatient department over a period of eight months she said that this defect has gradually improved, but, on close questioning, it seems more probable that she has become able to compensate for a still existing deficiency. The test results bear out this impression.

This patient further showed a very remarkable change: soon after the end of her treatment, when she came to interest herself in occupational therapy, she announced that she was no longer right- but left-handed. No great notice was taken of this statement at the time, as she was still far from well, but as she improved, it was found that she was using her left hand for things for which she had previously relied on her right. Now that she has been hard at work as a fur machinist for several months, she is gratified to find that she can get through a larger amount of work than formerly, as she is now ambidextrous. No neurological alterations were discovered to account for this phenomenon, the power in the right hand remaining unaffected. It may be supposed that there had been some sinistrality before.

These brief records indicate the type of memory loss which may follow convulsant therapy. Such loss is not a typical accompaniment or sequel of either depressive or schizophrenic states, although patients recovering from a schizophrenic attack like those in a depressive illness may complain of difficulty

in concentration or may show retardation on testing (Weitbrecht 1938, Schmorl 1938). In our cases it was not present before treatment with convulsants. There was no direct relationship between the severity of the psychosis and the degree of memory impairment noticed after treatment, nor was the age of the patient a significant factor. The fact that these defects were in most cases noticed and reported by relatives before being complained of by the patient would seem to rule out the possibility of their being the result of suggestion. As most cases in this series were given the same number of injections, it is not possible to say whether the number of convulsions affects the incidence of memory disturbances. The quantity and type of convulsant used is unimportant from this point of view. Not all the patients in the series complained of memory disability, and no impairment was demonstrable on testing in a certain number; this shows that some patients were more liable than others to suffer damage after this type of treatment. Possibly this difference is due to a relative inability of the vascular mechanism of some patients to withstand the sudden alterations in pressure caused by a convulsion. The finer delimitation of this hypothetical group is being investigated.

There is a similarity between the complaints of these patients and the memory disturbances that are so often seen after head injuries and in epileptics. Disturbances of the Korsakow type described by Plattner (1938) as arising after cardiazol treatment were not observed in our group. No human post-mortem material has as yet been reported on, but if lesions in the human brain are found, comparable to those observed in the brains of animals subjected to repeated cardiazol convulsions (Reitmann 1938, Dreszer and Scholz 1939), the existence of some organic intellectual impairment would not be at all surprising.

DESCRIPTION OF TESTS

The test employed was a modification of the Babcock test for mental deterioration (Babcock 1930). It is based on the assumption that a person's mental level indicated by a vocabulary test is likely to be little affected by organic impairment, whereas his mental level indicated by tests which require the application and organisation of knowledge to meet relatively new situations may be greatly lessened. When, therefore, there is a large discrepancy between his score in the two types of test, the vocabulary being, let us say, that of the normal adult, while the average mental level on the other tests is that of the normal child of eight, organic impairment is indicated: whereas if he obtains the score of a normal child of eight on both the vocabulary and the other tests, original defect is indicated. The test has, in fact, been used by Babcock and others in differentiating between mental deterioration and mental defect.

Subsequent work (Simmins 1933, Wittman 1933) has confirmed the validity of the vocabulary score as an indicator of original mental level, except in very severe cases of organic impairment.

When the test is given to schizophrenic and to manic-depressive patients, very little difference is found between the patients' scores on the vocabulary and on the other tests. The picture is hardly different from that of the normal person. The test, therefore, cannot be used to differentiate between "functional" psychosis and normality. Its main use appears to be as a relatively specific indicator of the presence of organic impairment, differentiating it on the one hand from original defect, and on the other from normality and functional psychosis.

Confirmatory work has been presented by Gilbert (1935), who compared the scores of 185 people in the twenties with those of 175 people in the sixties. The average score of the younger group on the vocabulary and on the other tests was identical, whereas that of the older group showed a difference of nearly five mental years in favour of the vocabulary test. Furthermore, Gilbert found that within the sixty-year-old group there was a significant difference between the scores of those under and of those over sixty-five, the difference being less in the younger patients, and pointing to a progressive deterioration within the decade.

The Babcock test, which was devised in America, is presented as a "battery"—that is to say, each test within the battery has been standardised independently of the others over a wide range of mental ages. It is not therefore necessary, when presenting the test, to use every item in the battery. Clearly, the more items one uses the more reliable will be the final average score, but some of the tests require a reconstruction (and a consequent restandardisation) before they are used on English people. The fact that each item has been independently standardised, however, enables one to dispense with these. Furthermore, some patients get tired or otherwise less coöperative after about three-quarters of an hour's testing. Consequently, in the experiment about to be reported, only the following tests out of the battery were used:—

1. Vocabulary.
2. Days of the week. (T)
3. Months of the year. (T)
4. Alphabet. (T)
5. Digits forward.
6. Counting backwards from 20 to 1. (T)
7. Immediate memory for a paragraph.
8. Woodworth-Wells substitution test. (T)
9. Digits reversed.
10. Knox cubes.
11. Days of the week reversed. (T)
12. Months of the year reversed. (T)
13. Memory for designs.
14. Memory for sentences.
15. Giving opposites of words. (T)

Tests marked (T) are scored on a time basis.

A further modification of Babcock's procedure was also employed. The rote tests numbered 2, 3, and 4 are tests of original knowledge rather than of application of knowledge to new situations. The average mental level in these three tests was therefore combined with the level in the vocabulary test, and the average of the two groups was taken as representing the original mental level. The average score on the remaining eleven tests was then compared with this.

If, for example, a patient had a mental level of 17 years on the vocabulary test, and of 18, 18, and 16 years on the three rote tests numbered 2, 3, and 4 respectively, the average level on the rote tests was 17⅓ years. This was combined with the level on the vocabulary test, and the average was then taken, giving a mental level of a fraction over 17 years. This figure was taken as representing the patient's original mental level. It will be seen that the procedure gives a greater value to the vocabulary test than to any single rote test. The vocabulary test is, in fact, regarded as being of equal value to the three rote tests combined. In this way the emphasis on the vocabulary test as an indicator of original mental level remains, but instead of having to depend entirely on this single measure one can add to its reliability by combining it with the average score on three other tests of early acquired knowledge.

An additional advantage of this modification of Babcock's procedure was that some tests scored on a

time basis were included in the tests of original level. This helped to differentiate cases of simple retardation from those showing impairment, for in this modification timed and untimed tests appear both in the indicators of original level and in the indicators of present level.

In the results shown in tables II and III a comparison is made between the scores on the modified Babcock test, as described above, of four groups of patients :—

(1) Schizophrenics who recovered without insulin or cardiazol treatment.

(2) Treated general paralytics.

(3) Epileptics (taken off sedative drugs for one week before testing).

(4) Patients treated with triazol or cardiazol.

No impairment was assumed when there was a difference of only 2 years or less between the tests

TABLE II—RESULT OF MODIFIED BABCOCK TEST BEFORE AND AFTER CONVULSION TREATMENT

—	Number in group	Original level (years)	Present level (years)	Result
Recovered schizophrenics	7	17½	16	No impairment
General paralytics	7	16	13	Impairment
Epileptics	9	12	8	Impairment
Cardiazol-treated patients	12	16½	13	Impairment

TABLE III—NUMBER OF PATIENTS IN EACH GROUP WHO SHOW IMPAIRMENT—I.E., THREE OR MORE YEARS' DIFFERENCE BETWEEN THE TWO GROUPS OF TESTS

—	No impairment	Impairment
Recovered schizophrenics ..	6	1
General paralytics	3	4
Epileptics	3	6
Cardiazol-treated patients ..	5	7

of original mental level and those of present mental level. A discrepancy of this order was regarded as lying within the margin of error of the test. If the difference was between 2 and 3 years, however, impairment was regarded as possible ; if between 3 and 4 years, impairment was taken as probable ; if between 4 and 5 years, impairment was almost certain ; and if over 5 years, the impairment was regarded as quite certain.

The numbers are small, but the tables agree in showing similarity between the general paralytic, epileptic, and cardiazol-treated groups, and a difference between these three groups and that of the spontaneously recovered schizophrenics.

RETESTING THE CARDIAZOL-TREATED PATIENTS

Of the cardiazol-treated patients, 7 were retested with the same test between three and seven months after their treatment had been completed, and 4 then showed less impairment or no impairment at all. The other 3, however, showed as much impairment on the retest as they had on the earlier test, performed soon after their treatment had been completed. In 1 of these 3 cases the retest was given as much as seven months after the treatment had been completed, in the second it was given six months after, and in the third, four months after completion.

It may be noted that the same test was given on both occasions. If there were any practice effect it would tend to lower the degree of impairment indicated by the retest. The fact that 3 of the patients continued to show impairment on retesting is therefore the more significant. It would be improper to conclude that the damage is permanent, but the evidence shows that it is not evanescent or negligible.

SUMMARY AND CONCLUSIONS

Of 16 cases treated with convulsants—comprising 12 schizophrenics, 3 depressives and 1 obsessional—13 recovered and 3 improved. Of these, 9 complained of memory difficulties which they maintained were due to the treatment and which in 5 cases were still present six months after cessation of treatment. A test confirmed the impression of organic intellectual impairment in 8 of the patients, though 2 of these did not complain of any disability. Susceptibility to the effects of convulsions seems to vary, for 3 patients did not complain of impaired memory, nor did they show impairment on testing.

Although the implications of this work are rather grave, it is doubtful whether they out-balance the value of the treatment in selected cases. The risk of memory impairment suggests however that convulsants should not be employed, except as an extreme measure, in patients whose livelihood depends on their memory and purely intellectual capabilities.

We wish to express our thanks to Prof. Edward Mapother for permission to work with patients under his care, and to Dr. A. J. Lewis for his criticisms and suggestions. One of us (J. M. B.) is indebted to the Medical Research Council for a part-time personal grant which enabled him to undertake this work.

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PAGET'S QUIET NECROSIS

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THE term "Paget's quiet necrosis," denoting a particular morbid process, has now almost passed from the realm of current usage. Despite this, its description persists in modern surgical textbooks, and occasionally a candidate in a viva-voce examination is asked for his knowledge on the subject. How far surgical authors have strayed from Paget's original description will be seen in the extracts selected from four modern and reputable volumes. Though the subject is not of vast importance, an attempted clarification may be of help.

Paget's original lecture was given in 1869 before the Clinical Society of London and published in the *Transactions* in 1870. He described the condition of a female, aged 19, who had had pain in her knee for one month. There was an oval swelling about 6 in. long nearly surrounding the middle of the shaft of the femur. Hard pressure over the swelling was painful. Otherwise the shaft appeared healthy. The patient was in the habit of breaking thick pieces of wood across her thigh. At no time was there any sign of fever. Operation was decided on, and a 6 in. incision was made over the outer part of the

thigh. All the tissues down to the periosteum appeared perfectly healthy.

"The periosteum was, in the portion, divided ⅛ to ¼ in. thick and in all its thickness, dense, tough, white and moderately vascular. Between the periosteum and the bone, the incision had laid open a flattened irregular cavity from which a little blood coloured fluid escaped, and was followed by the protrusion of some soft substance like coarse granulations. In this cavity which was from 1 to 1½ in. in diameter, was a thin rough sequestrum separated from the wall of the femur, about 1¼ in. long and ¼ in. wide. The walls of the cavity of which the outer was formed by the thickened periosteum and the inner by the hollowed out surface of the femur, felt smooth and velvety, as if covered by granulations, like those of ordinary cavities containing sequestra. The sequestrum appeared to be divided, not from the outermost layers of the femur, but from layers just within them."

Paget's comment on the lesion is as follows: "The central point of interest is, I think, in the fact of necrosis leading to separation of a bone, being unattended with inflammation of any of the features external to the periosteum, and with no more than a scarcely discernible amount of suppuration around the sequestrum."

Lawford Knaggs makes the following points about the process:—

(1) The sequestrum lies in a cavity surrounded by granulations but with a puzzling absence of suppuration.
(2) The sequestrum appears to be derived from the layers just within the outer surface of the bone.
(3) Both inner and outer surfaces of the sequestrum are eroded.
(4) Separation of the sequestrum may not be complete at the ends.
(5) The process may be extending at the extremities while the bulk of the sequestrum has separated.
(6) The initial lesion is probably a mild staphylococcal periostitis which becomes limited.

Paget's quiet necrosis is, therefore, a process of local necrosis and sequestrum formation in the superficial layers of the shaft of a long bone. The lesion is chronic from the beginning and affects mainly young adults. There is a minimal amount of suppuration surrounding the sequestrum, and sinuses are not formed. It is probably the result of a chronic osteitis due to a rather non-virulent staphylococcus.

In 1875 Paget, unfortunately, complicated the picture by his essay on Quiet Necrosis, published in his book "Clinical Lectures and Essays" in which he described again his original case and commented on two similar cases. He then suggested that by a similar process of "quiet necrosis" the formation of some of the loose bodies in joints might be explained. He wrote that some loose bodies "are portions of the proper articular cartilage, with or without some adjacent bone, which have suffered a 'quiet necrosis,' and been exfoliated into the cavity of the joint." He suggested trauma as the primary factor, and that the portion of bone was killed by violence and exfoliated without suppuration.

It is most probable that the lesion he was describing here was that now known as osteochondritis dissecans. Separation takes place into the joint without suppuration, but the loose body is not a true sequestrum, because it lives. We have not, in the ætiology of the lesion, advanced very far beyond Paget's original suggestion that trauma was a factor.

The following extracts from four modern surgical textbooks show the lack of unanimity of the authors and the confusion which may be caused in the mind of the reader.

(1) After a description of the late results of trauma to a joint with infection resulting in acute suppurative arthritis, "Articular cartilage tends to total destruction from ingrowth of pannus, from autolysis by the toxins in the joint and, once the underlying bone is exposed, by stripping off in flakes. Portions of the bone may die and form sequestra (Paget's Quiet Necrosis) whilst new bone is thrown out in other places."

(2) "Necrosis results from the following conditions (*a*) . . . (*b*) . . . (*h*) a variety, described by Sir James Paget under the name of quiet necrosis occurs as a result of direct injury, the sequestrum separating without suppuration. It is one of the causes of loose bodies in joints and especially in the knee, following a blow on one of the condyles."

(3) Quiet necrosis "was described by Paget as a process of local necrosis and sequestrum formation of a chronic character occurring in young adults. It is probable that his cases were examples of chronic osteomyelitis due to a rather non-virulent staphylococcus. The pathological process of exfoliation of outgrowths of synovial fringes and cartilage into joints he considered similar but the two conditions appear to be in no way similar."

(4) "Certain inflammatory bone formations may closely resemble osseous tumours although in the circumstances, the more diffuse character of the enlargement is likely to resemble an ossifying sarcoma rather than a simple osteoma. In this connexion the extraordinary deposit of new bone which may gradually occur round a small sequestrum is of great practical importance. To this condition Paget applied the graphic name of 'quiet necrosis.'"

The reader may judge the above extracts for himself in the light of Paget's original descriptions.

SUMMARY

(1) Paget's quiet necrosis is a process, not a disease. The process is one of local necrosis and sequestrum formation associated possibly with a traumatic factor.

(2) According to his original description the process took place in the superficial layers of the shaft of a long bone of a young adult.

(3) Suppuration is minimal, and sinuses are not formed.

(4) Paget later suggested that by the same process a portion of articular cartilage might be exfoliated into a joint and produce a loose body. This probably corresponds to the lesion which we now call osteochondritis dissecans.

. . . "Be an anthropologist, Reeves. Fish up a lot of facts, alleged on very doubtful authority, about primitive man—his marriage ceremonies, his burial customs, his system of land tenure. Look at the whole mass of facts squint-eyed until you can see a theory in it. Embrace the theory, trot out all the facts which support your theory; write a long appendix on all the facts which contradict your theory, showing them to be insignificant or irrelevant, and there you are.

"Is there any money in it?

"No. If you're out for that, I should take to psychoanalysis. The system's the same, generally speaking, only instead of dealing with primitive man, whom you can disregard because he isn't there, you are dealing with a living man, who will probably tell you that you are a liar. Then you tell him that he is losing his temper, which is the sign of a strong inhibition somewhere, and that's just what you were saying all along. The beauty of psychoanalysis is that it's 'Heads-I-win-and-tails-you-lose.' In medicine your diagnosis of fever is a trifle disconcerted if the patient's temperature is subnormal. In psychoanalysis you say, 'Ah, that just proves what I was saying.'"—RONALD A. KNOX, "The Viaduct Murder" (London, 1939).

MEDICAL SOCIETIES

MEDICO-LEGAL SOCIETY

AT a meeting of this society on June 22, with Dr. G. ROCHE LYNCH, the president, in the chair, a discussion on

The Psychiatric Handling of Delinquents

was opened by Dr. DENIS CARROLL. He said that psychiatric advice should not be given without a careful study of the offender under suitable conditions. The selection in court of suitable offenders for investigation was difficult even for a psychiatrist. The presence of a psychiatrist in court, and more systematic instruction of magistrates and probation officers, offered a possible solution. It would not be practicable to employ a psychiatrist in every court, and, generally speaking, the selection must be made at once, as not all offenders could be remanded. As research indicated the necessary diagnostic criteria it might be possible to mark certain obvious types of offenders as worth routine remand, so that the probation officer might obtain data to define the need for medical investigation. Some groups might even be found worthy of routine medical examination—e.g., drug-addicts, young chronic alcoholics and some sexual offenders. The provision of the Criminal Justice Bill which allowed the question of the mental treatment of an offender on probation to be raised at any time during the first three months of the period might provide a solution in many cases.

Dr. Carroll described the psychiatric investigation, which is usually carried out by a team consisting of psychiatrists, psychologists and specially trained social workers. The psychiatrist conducts a full mental examination, and either he or a general physician examines the offender physically. The psychologist, often a non-medical expert, estimates intelligence and ability for certain types of work by a carefully constructed set of tests. The social worker obtains a full history of the offender's past life, environment, family and other circumstances, visiting the relatives and friends. Dr. Carroll said that much of this work could be done by the probation officer if properly trained, but he would find it difficult to give the necessary time. The ideal is to employ a social worker who has been a probation officer. An hour each for the doctor and psychologist and two hours for the social worker is usually long enough. There is serious lack of provision for inpatient observation; special centres, both official and non-official, are required. The bill will help by empowering the local authorities to set up, or subscribe to voluntary bodies setting up, certain types of observation and treatment centres. Some offenders object to repeated visits for investigation, and difficulties arise when the offender has to be accompanied to the clinic. In practice these difficulties are handled successfully by obvious modifications of the investigation and by tact. Some of the difficulties would be eased if the non-attenders and objectors were remanded in custody or for inpatient observation, but it is not always possible to know when troubles will arise. They are usually due to the deep-seated hostile or persecutory attitude of mind characteristic of certain types of delinquents.

After the investigation a report is sent to the court embodying the important findings, explaining their relation to the offence, and suggesting what should be done by way of treatment—where it could be carried out, the need for supervision, and so on. If possible some forecast of the future is included. The general treatment is that of the causes, which are multiple and can be grouped under the heads of clinical, sociological and psychopathological. The clinical state includes such factors as organic or mental disease, the degree of intelligence, pathological personalities, emotional stress, and habit of crime. Sociological factors include bad or broken homes, bad companions, unsuitable work or occupation, economic stress and temptation. They are apt to be given too much importance, for they produce delinquent behaviour only in a person otherwise predisposed. Psychopathology includes all the underlying mental processes, some of which may produce delinquent behaviour in so-called normal types. The various theories can be turned to direct account in prescribing and carrying out useful treatment. Many of the mental mechanisms prescribed by the freudian school are widely used by non-freudian psychiatrists in treating delinquents. Psychoanalysis of offenders should be carried out only by trained analysts, and the theoretical teaching of the various schools of thought should be applied only to those cases where it is known to be of value.

When advising or supervising sociological measures, Dr. Carroll continued, the psychiatrist should bear in mind any contributory factor the persistence of which is likely to result in further delinquency. Several methods may have to be employed at the same time and several people may be involved, and it is highly important to maintain contact between them. A good social worker is invaluable and can carry out much of the necessary treatment of parents and others. Treatment must be adequate, and training or supervision must be thought of in terms of years rather than months. It is important to obtain full knowledge about any place to which the offender is sent, for success depends largely on the personnel of the institution or foster-parent. Training implies general character training and the development of a sense of social responsibility, as well as training in some form of employment. Of psychological methods, suggestion is of more use with juvenile offenders than with adults. Re-education is especially valuable in milder personality deviations. Some workers favour moral education, especially for normal offenders. Persuasion is a useful weapon with the intelligent and weak type. Probation work is very encouraging; there is no difficulty in combining it with other methods, even intensive psychotherapy. The criterion of whether psychotherapy should be used is whether the emotional state which has developed calls for such special skill to resolve it.

The outlook for people who have committed isolated or accidental offences is good unless they are clumsily handled, but a delinquent habit is very difficult to eradicate. The younger the offender the better the prospect. The environment may be so bad that nothing short of segregation is any use. The attitude of the offender to society is always a mixture of friendly and unfriendly feeling, and the greater the capacity for forming positive transferences to the outside world the better the prognosis. The effect of punishment is not easy to forecast. In some types it is disastrous, and the serious juvenile offender is generally better treated without it. There is scope for the application of common sense. Many cases can be dealt with simply and rapidly, but the psychiatrist does not often see these—a tribute to those who select his cases.

DISCUSSION

Dr. NORWOOD EAST said that of 2311 offenders placed on probation within his knowledge, 70 per cent. did not commit an indictable offence in the next three years. Of 438 persons who had already committed an offence when placed on probation, 54 per cent. did not commit a further offence for three years. In about 70 per cent. of cases ordinary penal methods contributed to success—a far better result than any claimed by psychotherapy. Petty-sessional courts heard about 99 per cent. of all charges: in this country crime is not a menace but merely a nuisance. Psychiatric treatment includes general medical treatment, and much can be done by diet and drugs, occupation and good companionship, and regulation of the daily routine. There is nothing to hinder the prisoner from receiving necessary psychotherapy from the prison medical officer. Most sexual offenders have a fixed habit of delinquency and are unwilling to be reformed. Nevertheless, even if psychiatric treatment is not successful it may be useful in providing data for research into the fundamental basis of crime, especially of abnormal crime. In adult cases investigation is more useful than treatment.

Dr. ALEXANDER BALDIE complained that psychotherapists are in some quarters rather improperly regarded as mystics and supernaturals. The "court psychiatrist" does not yet exist. A psychiatric observer or assessor, he said, would be of the greatest value not only to the court, but also to the hard-worked prison officer and to others who are dealing with the disposal as well as the treatment of the offender. It is deplorable that in the London courts, the stipendiaries of which are unequalled for their competence, so many offenders with pronounced psychopathic traits should go through the machinery of trial and disposal with their condition unrecognised through lack of means to bring it to the court's attention. It would greatly assist the court in determining factors mitigating the offence if these psychopathic traits could be recognised.

Dr. J. C. M. MATHESON declared that on the evidence of the figures the problem is not so great as might at first sight appear. He doubted whether psychiatrists have passed the student stage and are yet able to recommend treatment for delinquency. Perhaps the present suggestions are to a certain extent tentative. The public should be told that very little is yet known, and that psychiatrists are still groping their way. Progress would better be made by approaching the problem as students rather than as therapists. The psychiatric adviser to the court might usefully bring to the court's notice certain abnormal features in persons charged.

REVIEWS AND NOTICES OF BOOKS

The Englishman's Food

Five Centuries of English Diet. By J. C. DRUMMOND, D.Sc. Lond., professor of biochemistry, University College, London; and ANNE WILBRAHAM. London: Jonathan Cape. 1939. Pp. 574. 12*s.* 6*d.*

THIS well-printed and illustrated book makes fine confused feeding, as Dr. Johnson is reputed to have said of the haggis. It is a book more to be dipped into or browsed on than read straight through—it would make a fine bedside book for a dietitian. The authors have spread their net wide and taken in poetry, political pamphlets, medical treatises, diaries, estate accounts, novels, herbals, and books on husbandry and gardening in their quest for evidence of what England has eaten down the ages. The study is fascinating, though the reader may at times weary of the digressions and the sudden jump from topic to topic and from century to century. The book would have been better if it could have been compressed and kept more chronological. None the less it will be a rich delving ground for all interested in dietetics for years to come.

The authors bring out how surprisingly slowly new foods make their way into a country, although no Elizabethan would recognise half the foods that we eat today. The medieval garden had no fruits but apples, cherries and plums, if we except the grape of the monastic vineyard, and few vegetables except garlic, onion and leek. Fruits were not thought wholesome till 1750. Potatoes were introduced in late Elizabethan days but medical opinion was against them, and they did not appear in books on gardening till 1726 and were not taken up by the Board of Agriculture till 1790. Bananas were actually introduced into this country in the eighteenth century but were not a common article of food till the beginning of the twentieth. Why then were deficiency diseases not rife? The answer is that they were. Scurvy was a common disease in 1500, though by 1597 cresses and lemons were recognised as specifics, and Culpeper says that parsley and strawberries are "good to fasten loose teeth." There is evidence that vitamin A was deficient, for night-blindness and stone in the kidney and bladder were common. Rickets too was rife in the Low Countries and North Germany in the fifteenth century, and sixteenth-century painters showed the holy infant as a rickety baby.

We see here what a debt this country owes to religious and political refugees in the importation of new foods, particularly from Holland. Royal marriages acted in the same direction. On the other hand, snobbery, or the desire to imitate the upper classes, militated as it still does against the adoption or retention of a sound diet. The last two chapters, called "The War" and "A New Era," will stimulate those who think nutrition the foundation of the national health to press forward their demands for a consistent and progressive Government food policy both in war and peace. In five centuries our food has made great advances, but it is by no means satisfactory yet. If this book shakes the complacency of the "not inconsiderable proportion of the higher ranks of administrative officials" it will have done good.

Trauma and Internal Disease

By FRANK W. SPICER, A.B., M.D., F.A.C.P. London: J. B. Lippincott Company. 1939. Pp. 593. 35*s.*

THE relationship of injury to pathological conditions is of great practical importance in a world in which both injuries and the litigation they lead to seem to be getting more and more common. Only in the case of certain obvious surgical lesions, such as wounds, can it be asserted with complete confidence that the cause must be violence and could not possibly be anything else. When there is a tumour, diabetes, or a chronic affection of the central nervous system, there may be, in the words of the late Lord Balfour,

"every gradation from absolute certainty through practical assurance down to faint possibility."

Dr. Spicer of Minnesota set out to study the literature of the traumatic factor in disease, a subject which he thinks has been rather neglected in the standard textbooks, and he presents a formidable bibliography, but he shows an indifferent critical faculty in extracting his material. In fact, he seems to have sought authority for asserting that almost every imaginable disease may be due to, or at least aggravated by, injury. The case-histories he quotes are often interesting but their evidential value is sometimes flimsy in the extreme. For instance, a man sustained an electric shock, after which "the nurse . . . states . . . that the pulse was markedly irregular and rapid. The man apparently made a complete recovery." On this evidence Dr. Spicer concludes that electric shock may cause auricular fibrillation.

This mass of material was not collected without great industry on the part of the author, and it seems a pity that more discrimination was not used in its presentation.

Crystalline Enzymes

The Chemistry of Pepsin, Trypsin and Bacteriophage. By JOHN H. NORTHROP, member of the Rockefeller Institute for Medical Research. New York: Columbia University Press. 1939. Pp. 176. 15*s*.

THIS is a valuable book, for the author has been associated with the crystallisation of enzymes from its earliest days, and he has made a full review of the whole field of study. He gives a detailed description of the crystallisation of trypsin, chymo-trypsin, pepsin, pepsinogen and the various peptidases. Hitherto most of this material has had to be sought for in the German literature or in the original papers of Northrop himself and various other American writers. It is here set out conveniently and concisely, with a full bibliography and an excellent index.

Diagnosis and Treatment of Diseases of the Thyroid

By JAMES H. MEANS, M.D., Jackson professor of clinical medicine, Harvard University; and EDWARD P. RICHARDSON, M.D., John Homans professor of surgery in the university. London: Humphrey Milford, Oxford University Press. 1939. Pp. 367. 21*s*.

THIS volume of reprints from the Oxford Monographs on Diagnosis and Treatment contains much of value to both physician and surgeon. After a chapter on the historical aspects of our knowledge of the thyroid gland, there are useful summaries of the function and diseases of the gland, and of the principles of diagnosis and treatment. The classification is not always clear. Diffuse non-toxic goitre is discussed under colloid goitre, and diffuse toxic goitre and nodular toxic goitre are treated as two distinct conditions, under exophthalmic and adenomatous goitre, in spite of the statement in the text that true neoplasms or adenomata are not always present in the latter. The diagnosis and treatment of these conditions are dealt with systematically, but the rarer complications, such as exophthalmic ophthalmoplegia, postoperative exophthalmos, osteoporosis and so on, receive little attention. Myxœdema is considered thoroughly, but the varying grades of hypothyroidism are ignored. Throughout the book there are excellent illustrative case-reports showing the results of treatment, but more definite guides to ultimate prognosis would be welcome. If the reader expects, as he well might from such authorities as these, a discussion on the recent advances in knowledge of the physiology and functional pathology of the thyroid, he will be disappointed. But he will find the book an admirable practical guide to diagnosis and treatment.

Bacterial Metabolism

(2nd ed.) By MARJORY STEPHENSON, Sc.D., associate of Newnham College, Cambridge; member of the scientific staff of the Medical Research Council. London: Longmans, Green and Co. 1939. Pp. 391. 21*s*.

THIS monograph first published in 1928 has doubled its size, and appears now as "an advanced textbook." The treatment of the subjects is amplified; important additions concern bacterial growth and nutrition, bacterial enzyme systems, nitrogen fixation and the newly opened field of bacterial photosynthesis. The metabolic activities of bacteria are of moment in a great deal of medical, industrial and agricultural bacteriology, but from the vast range of phenomena in these fields the author has selected only those that can profitably be discussed in the light of modern biochemistry. For this reason the textbook will probably be more useful to advanced biochemists than to bacteriologists. Facts are for the most part allowed to speak for themselves, and there are few concessions to the uninstructed. In scope the book has the stature of a textbook; in presentation it has not advanced sufficiently beyond the monograph written for experts. Nevertheless, the medical bacteriologist will find it a mine of digested and documented information, and, what is perhaps more useful, a graveyard of a number of doubtful hypotheses.

Our chief complaint is of the paucity of general comment, which is the more regrettable because Dr. Stephenson is highly illuminating on the rare occasions when she allows herself something more than a rigidly ad-hoc criticism of her material. The book avoids being a series of detached essays on different aspects of bacterial metabolism by a process of historical dove-tailing, but little evidence of any general attitude to the subject is allowed to emerge unless it be a conviction that empiric bacteriology is to be regarded merely as an addition to the complexity of nature. Perhaps the subject is scarcely ripe enough for generalisation. At any rate, until Dr. Stephenson thinks that it is, we must be content with this excellent interim report.

Penn'orth of Chips

Backward Children in the Making. By CHARLES S. SEGAL. London: Victor Gollancz. 1939. Pp. 128. 3*s*. 6*d*.

DESPITE the title this book is a serious contribution to social science. It gives the results of Mr. Segal's own experiment—the detailed examination of the environment of 26 boys in a backward class. The observation that dullness and poverty are closely associated is strikingly illustrated. Mr. Segal does not, however, confine himself to the task of demonstrating that these two evils are associated; he is at pains to show to what a large extent poverty must be considered the cause of dullness. In doing this the whole body of evidence is taken in review and the opinions of dietitians, psychologists, social workers and others who have devoted time and labour to the subject are freely quoted. The book in fact, though not large, is a compendium of information of interest to doctors as well as laymen. There is a valuable preface by Dr. Cyril Burt.

THE LANCET

LONDON: SATURDAY, JULY 1, 1939

FUNDAMENTAL CANCER RESEARCH

ON Tuesday afternoon the new laboratories of the Imperial Cancer Research Fund at Mill Hill were formally opened, within a stone's-throw of the new central institute of the Medical Research Council. In an address, with which he made the occasion additionally memorable (see p. 33), Sir Gowland Hopkins recalls the confusion and pessimism in the medical profession on the subject of cancer which prevailed when the fund was established in 1902. Now the fund has a scientific tradition based on nearly forty years of research by a laboratory staff organised with far-seeing wisdom as a working unit. Under the direction of Bashford and Murray this unit has laid stepping-stones in the systematic study of cancer by experimental means. Galling as must have been the straitness of its accommodation in Queen Square to the personnel, Dr. Gye will recognise the advantage of having waited for a worthier home until the needs of research were well established and the means available to equip an institute capable of supplying them. It was certainly time for the fund to do something for its own staff, for there are few laboratories in Great Britain which have not depended for scientific material upon its generosity.

The suggestion to found an institute for the investigation of the nature, cause and treatment of cancer originated (as the late Sir Frederic Hallett tells us in the first report of the fund) in 1901 "in some conversation between a private gentleman and a member of the council of the Royal College of Surgeons of England." Sufficient funds were quickly collected to enable investigations to be started, and the new organisation was placed under the joint control of the Royal Colleges of Physicians and Surgeons. From the start it was realised that before ever the experimental study of cancer could, with profit and with hope of carrying conviction, be inaugurated it was necessary to gain a conception of the extent and distribution of cancer, and to clear the ground of the dogmas that cancer was a disease limited to civilised man and that it was increasing at an alarming rate. Accordingly, with the help of Dr. John Tatham of the General Register Office and of the large London hospitals, an examination of the statistics of cancer was undertaken. Arrangements were made with the hospitals to check the accuracy of the diagnosis of cancer in a series of 10,000 cases according to the accessibility or inaccessibility of the site of the tumour, and when this was done a striking difference came to light. In the accessible sites only 9 per cent. had not been recognised clinically, while 7 per cent. had been erroneously diagnosed as cancer. In the inaccessible sites the percentage of missed diagnoses was as high as 38, while only 9 per cent. of cases had been erroneously diagnosed as cancer. Similar investigations in the United States and on the Continent have since had similar results. Even under conditions most advantageous for diagnosis the number of cancer cases not recognised is surprisingly high for the inaccessible sites; since these are responsible for a large fraction of the whole cancer mortality, the recorded total must be sensibly lower than the actual one. When therefore a comparison of the total recorded mortality is made over long periods, we must expect the improvements in methods of diagnosis, and the greater attention paid in recent times to the clinical recognition of cancer, to diminish the number of missed diagnoses and thus increase the recorded mortality. If this argument is correct the increase in mortality will be found to fall mainly upon the inaccessible sites—and a glance at the Registrar-General's reports since 1901 proves this to be so. Up to the beginning of this century the official figures were not sufficiently detailed to admit of a comparison between accessible and inaccessible sites. By arrangement with Dr. Tatham provision was made for a more detailed analysis, and in the report for 1903 the cancer cases were classified according to sex, age and parts affected. "The arrangement of this column," it was stated in a footnote, "has been fixed after consultation with Dr. E. F. Bashford, director of the Imperial Cancer Research Fund." Thus it was established that cancer is not increasing at an alarming rate in civilised communities and for this contribution to our knowledge we have to thank the fund.

During this time the fund, with the generous help of Joseph Chamberlain, was making inquiries about the existence of cancer among the primitive races of the British Empire. It was found that almost every kind of cancer known in civilised countries could be duplicated among peoples scarcely touched by what is called civilisation. This put an end to another of the dogmas which was inhibiting a rational investigation of cancer. A third belief widely held was that cancer is rare in animals; but it is a characteristic of cancer that it is uncommon in the younger age-groups, and Bashford found that when animals were allowed to complete their normal span of life cancer was often observed. The most satisfactory animal for this purpose is the mouse, being short-lived and kept easily in large numbers. It was found possible to establish mouse data, of greater accuracy than human statistics, which showed a cancer incidence rising with increasing age just as in man. Up to 1900 no single cancerous mouse had been found in this country; before the fund had been in existence many years, over 1000 cases of cancer in mice had been observed and diagnosed microscopically. With veterinary help the search was extended to all domesticated animals, when cancer was found wherever it was looked for properly. "Cancer," remarked Bashford in his second report, "has been discovered to pervade the whole vertebrate kingdom."

The experimental study of cancer on a broad basis now became possible; it was certain that observations on cancer in animals have relevance to cancer in man. The age-incidence, the mode of origin, the structural characters, the manner of growth and dissemination through the body, and the almost invariably fatal ending were found to be the same throughout the animal kingdom. In no other disease in fact is there such close identity as between cancer in man and cancer in animals. All subsequent experience has verified these early findings of the Imperial Cancer Research Fund. They are now buried in the body of our knowledge of cancer and it is right that they should be recalled at this moment in the fund's history. Since those early days great progress has been made. Carcinogenic substances have provided the opportunity to study the inception of cancer; refinements of biochemical technique now enable the chemist to measure the metabolism of the malignant cell; and the discovery of virus tumours by Peyton Rous has given the hope that the discovery of the proximate cause of cancer is not beyond the wit of man. In all these advances the fund has played its part and whatever direction cancer research may take in the future will be profoundly influenced by the work which the fund has already accomplished. The courage and the initiative are there; those who wish the fund well will be content to leave its intellectual freedom completely unfettered.

THE DECLINE IN FERTILITY

THE prospects of a fall in our population, which are causing perhaps too much concern in some quarters and not enough in others, were discussed at length in the House of Lords on June 21. Lord SAMUEL set out the grounds on which the familiar hypothetical estimates have been made and painted a dismal picture of the economic and strategic results that must follow if the estimators prove true prophets. The immediate cause, he said, is no physiological change in the human race but deliberate conscious human action—children are not born because prospective parents do not wish them to be born. The primary cause is largely economic—namely, poverty or the fear of poverty, and consideration of the nutritional, educational and general interests of the children already born. He set no value on treatment of the immediate cause, but, backed by Lord DAWSON, Lord DERWENT and the ARCHBISHOP OF YORK, demanded treatment of the primary disease, by the institution of family allowances. Lord DAWSON put forward, too, the need for parental educational measures to allay the fears of maternity and bring home to mothers and fathers the ultimate wisdom of larger families. Lord SAMUEL and those who came after urged the Government to set up a Royal Commission on fertility, but Lord STAMP, and later Lord TEMPLEMORE for the Government, pointed out that such a commission would have few real data to work on.

The Population (Statistics) Act, which came into force a year ago, will elicit much about human fertility, but many problems outside the scope of figures will remain. Vital statistics, for instance, may tell us what proportion of women who die are childless and how many have had children; but they will tell us nothing of the factors responsible for sterile marriages and little of the influences which induce married couples to restrict their families. A proportion of marriages, we will learn, are sterile. What proportion of these are childless involuntarily or by design? The information obtained by registrars of births, marriages and deaths will throw no light on these intimate questions. In the complex of influences and experiences which deter from parenthood, medical factors play a definite, though as yet unascertained, part. It may be impossible to consummate a marriage owing to various causes affecting both sexes: varying degrees of sterility may be present in either parent; the woman may have had a number of miscarriages or stillbirths; she may suffer from one of many physical abnormalities or chronic illnesses which make pregnancy dangerous or incapacitate her from devoting proper care to her children in their early years; the father's bad health may weaken his earning power or cause misgivings as to his occupational stability, thus taking shape as an economic deterrent from parenthood; lastly, though physically and economically equipped for having children, the couple may hesitate to embark on parenthood because of hereditary defects (real or imaginary) in their ancestries.

The prevalence and importance of such factors as these can only be elucidated by direct inquiry. On another page appears a letter from representatives of the Population Investigation Committee, asking the coöperation of our profession in an inquiry which will bring out facts, on these and other matters, to take the place of the present guesswork. They should meet with a ready response.

WHY FLOGGING SHOULD BE ABOLISHED

PARLIAMENTARY voting on the proposal for the abolition of corporal punishment by order of a court is, we understand, to be treated as a non-party matter, and discussion has been sufficient for current arguments for and against it to be clearly defined. The report of the Departmental Committee on Corporal Punishment provides decisive evidence disproving the assumption that such punishment has any deterrent effect upon the person punished, and some evidence pointing to the likelihood that it has an opposite result. The supposed deterrent effect upon would-be criminals is incapable of such close examination, but oft-quoted positive claims in that direction did not survive statistical inquiry by the committee. It seems, therefore, that there is enough material in the report, when studied as a reasoned statement of cause and effect, to enable our legislators easily to reach a conclusion favourable to the proposal. Yet such a conclusion is by no means certain; as Mr. WILFRED TROTTER said in our columns last week, we cannot separate off the reasoning process as such and set it to work in an emotional vacuum; and opponents of the proposal

frankly appeal to emotion in calling for retribution to satisfy the feeling that those who commit especially horrible crimes should suffer in their own bodies. To this emotional appeal there is no easy answer; if we frankly decide to let our feelings overwhelm rational judgment how can our claim be resisted?

It is curious that sexual crimes are so often specified as calling for bodily punishment, for a very serious objection to the purposeful infliction of physical pain, by law or otherwise, is the close connexion of such an act with perverse sexual manifestations, a connexion which is rarely enunciated in plain language. It is not a matter of unconscious sadism (the existence of which need not come into consideration at the moment) but of conscious sadism which accounts for cases of apparently senseless cruelty and reaches its acme in the lust murders with which our newspapers make us familiar. Short of such horrors there exists, among the sex perversions that our civilisation seems to produce, a capacity for receiving a sexual stimulus from the contemplation, in reality or fantasy, of the infliction of pain. This capacity is known in early life, often before the nature of the stimulus is recognised by the unfortunate child, and many an adult, who would greet with alarm and admonitions a manifestation of normal sex development in a child, acquiesces in a punitive performance that may actually stimulate a tendency to abnormal sex development. When matured, this sadism may in either sex express itself in masturbatory fantasies, or the sexual orgasm may be dependent upon the actual or symbolic performance of sadistic acts. Medical psychologists find that patients under treatment for various troubles will describe how, perhaps against their will and in spite of their abhorrence, accounts of the wilful infliction of pain will sexually stimulate them; those who, acting voluntarily or under inner compulsion, seek a sexual orgasm by the infliction of severe bodily pain or actual injury on another, are likely to fall, and often do fall, into the hands of the law. One hears of the provision of whips in brothels, and the existence of a literature of flagellation appealing to perverts is well known, some of it being disguised and some openly sexual.

The incidence of the conditions here briefly described cannot be closely estimated, but those who know enough to recognise them know also that, in varying degrees of intensity, they exist unrecognised all around us. Allowing validity to the emotional appeal, we must admit it is horrible to think that anyone affected by such tendencies should come in contact with legalised floggings, but there are no means of preventing it. The stimulation of the normal sex instinct is ever an object of control and censorship; much worse is the stimulation of one of the most distressing perversions of that instinct, which is inevitable as long as flogging is a part of our legal equipment. We must bear in mind those who may be harmfully affected by the discussion or the description of deliberate infliction of physical pain.

ANNOTATIONS

WANTED—BLOOD-DONORS

AN extensive appeal for volunteer blood-donors is to be launched by the Ministry of Health, in coöperation with the Medical Research Council, next week. The appeal is for the depots which will serve civilian casualties in London and the Home Counties in time of war; plans for the rest of the country are being made locally. A blood-supply officer has been appointed to each of the sectors into which this area has been divided, and his duty will be to see that every hospital in his sector, especially those in the central area, could be provided with adequate amounts of blood for transfusion. For this purpose a number of stations for empanelling donors have been set up and will be open daily from 10 to 12 A.M. and from 5 to 8 P.M. from July 3, on six days a week. Volunteers on registration will be grouped, and those who are universal donors will receive a card telling them where to report if an emergency arises. Volunteers of other groups will receive cards thanking them for their offer of help and letting them know their blood-groups, in case they should themselves need transfusion. Blood will be withdrawn from universal donors immediately war is declared, and stored at temperatures of 2°–4° C. until required. It is reckoned that 100,000 volunteers will be needed in the London area.

Experience in Spain showed that the collection and storage of large quantities of blood for transfusion was carried out most successfully in specially equipped clinics with adequate plant for refrigeration and sterilisation. Four such depots, at Maidstone, Luton, Slough and Worcester Park, are now being equipped for the storage of about 1000 bottles each, with the necessary apparatus for collecting and administering blood. Blood will be distributed from these centres by refrigerated vans. The sites have been chosen because they contain a relatively large population at a reasonable distance from London and are served by a good road system. Each depot is expecting to collect a panel of 20,000 volunteer donors, of whom about 8000 will be universal donors. About 10,000 donors have already been tested. Any healthy person between 18 and 65 is considered suitable to volunteer and for obvious reasons it is hoped to enrol as many women as possible. The addresses of centres where preparations have already been made for enrolling volunteers will be announced in the next few days.

THE CARDIAZOL FIT

SINCE desperate diseases call for desperate remedies, psychiatrists were not disposed to reject the new treatment of schizophrenia by insulin and by Cardiazol because these methods, when first seen in action, did not particularly commend themselves as safe and agreeable. There were however differences in these respects between the two methods. Cardiazol had a certain advantage. *Tuto* might be dubious, and *jucunde* definitely not the case, but so much weight could be put on *cito*, as it seemed, that the drug came to be widely employed, even in the wards of general hospitals, and on a variety of psychiatric disorders. Dislocations of the jaw, an occasional

fractured femur—these were not taken too tragically, since the great benefits hoped for would outweigh them. Whether this is so cannot yet be decided, but graver complications are now reported. On p. 17 of this issue Dr. Tooth and Dr. Blackburn publish evidence that the cerebral changes occurring during a cardiazol fit may give rise to impairment of intellectual capacity and memory. This would be a high price to pay especially if the patient depended on his intellect and memory for his livelihood. It is excessively high when one considers that the "spontaneous" remission-rate in schizophrenia is, in any case, not much below that claimed for cardiazol treatment. Gelperin,[1] in a recent communication, reports 94 schizophrenic patients who were discharged improved out of a total of 235 admitted to a psychiatric ward, though they had had no other treatment than superficial psychotherapy. This would dispose of the argument sometimes put forward that a little hebetude is better than a chronic insanity. Both the chronic insanity and the hebetude can be averted in the case of many schizophrenics if the psychiatrist can afford to be patient and satisfied with the general psychiatric methods that were available before cardiazol and insulin had been introduced. Tooth and Blackburn are cautious in their inferences and would not damn the cardiazol method outright because of its occasional untoward results: but the difficulty is to know which cases are the right ones to select for it. The deterioration they report, remarkably confirmed by psychological testing, is not the only complication of cardiazol treatment. The high incidence of vertebral fracture in cardiazol-treated patients has recently been noted in America.

PRIVATE WARDS FOR CHILDREN

IT is said that when a certain royal personage was ill his surgeon assured him that he would be looked after as well as if he was a hospital patient, and he was comforted. Some such thoughts must have been in the minds of the management committee and medical staff of the Hospital for Sick Children, Great Ormond Street, in their rebuilding, for in providing private wards on the seventh floor they seem to have set out to give the child whose parents can afford to pay for it as happy and as profitable (in the health sense) a time in hospital as his poorer brothers and sisters in the floors below. There are single-cot rooms, which can be curtained off for privacy or opened into one another to provide for a nanny or other social amenities, for twenty children, and two small wards of four cots each provide that type of companionship in disease which is so often of great disciplinary value in treating minor behaviour problems. Each room opens on a large balcony, well protected by railings and wire netting, with an unrestricted south aspect to let in sun and air. While forming an integral part of the whole hospital and thus sharing in all the modern services available—with oxygen on tap, mobile electric lamps and other accessories—the private floor has its own entrance, waiting-room, consulting-rooms and operating-theatre. Rooms are set aside for nursing mothers, and "at the absolute discretion of the medical staff" single rooms, if available, may be used for mothers and nannies. It is probable that in this phrase quoted from the regulations lies the greatest advantage of the hospital over the home in the treatment of the sick child. Handed over to the care of skilled nurses accustomed to humouring and amusing the sick child on a basis far removed from that of the home nursery, the small patient makes quick adjustments which are only slowly reached, if ever, in the atmosphere of a home upset by the advent of illness. For surgical procedures such a programme has obvious advantages, and for the many medical disorders in which a psychological process is playing a dominant or even subservient part the complete change in environment, human as well as physical, produces results which have long been recognised among the ordinary hospital patients. Great Ormond Street is not the first children's hospital to open accommodation for private patients, but thanks to the generosity of Lord Nuffield it has been possible to incorporate in the rebuilding scheme a unit which should serve as a model of its kind.

1. Gelperin, J., *J. Amer. med. Ass.* June 10, 1939, p. 2393.

A COLLEGE FELLOWSHIP IN CLINICAL SCIENCE

WITH the inauguration of a department of medicine the opportunities at Cambridge for clinical and correlative research work are now greatly improved. But whereas numerous college fellowships in the past have been available for graduate students of physiology and pathology there has hitherto been no recognition of clinical science as an appropriate subject for a fellowship, partly because facilities were lacking and partly because clinical science was not yet accepted as worthy of inclusion among the other natural sciences. This acceptance is now becoming general, and the announcement that a Stringer fellowship at King's College may on this occasion be awarded to a candidate whose study or research falls within the group of subjects including clinical medicine marks a further stage in the development of scientific medicine at Cambridge. For a man of suitable qualities the prospects and amenities of the appointment should offer strong inducements. Candidates must be members of the university, under thirty years of age on Dec. 6, 1939. Any candidate who is in doubt if his study or research falls within the prescribed group should consult the Provost, to whom applications should be sent by Oct. 16.

ASEPTIC NECROSIS OF BONE

WHEN the pressure in a diving-bell is reduced too suddenly gas is liberated from the tissues more quickly than it can be removed by the blood, and the symptoms of caisson sickness may result. In discussing the aseptic necrosis of bone that sometimes follows, and quoting four cases with autopsy or biopsy findings, Kahlstrom, Burton and Phemister [1] point out that when the body is exposed to high atmospheric pressure the gases of the air are absorbed in different degree according to the nature of the tissues. Thus fat or lipoid tissue such as the nervous system absorbs about five times the amount of nitrogen that water or serum will take up, and it is such tissues that are likely to be most damaged by the liberation of gases during decompression. Oxygen is relatively easily dissolved and got rid of, but the bubbles of nitrogen set free in the fatty marrow of long bones give rise to emboli which may obstruct end-arteries and produce necrosis. If this necrosis affects the bone bordering a joint the weight-bearing portions of the bones may collapse and there may be lesions of joints, sometimes with the formation of intra-articular foreign bodies. This process lends support to the view that arthritis deformans, in which the lesions are much the same, may be due to

1. Kahlstrom, S. C., Burton, C. C., and Phemister, D. B., *Surg. Gynec. Obstet.* Feb. 1, 1939, p. 129.

vascular blockage and necrosis of the bone underlying articular cartilage.

In a second paper [2] these American authors describe massive multiple infarcts of bones arising without exposure to compressed air. The pathological and radiological appearances in some cases closely resembled those following caisson sickness. The ætiology of these infarcts is obscure, but the authors suggest that they may be related to the idiopathic lesions sometimes seen in late childhood. It also seems possible that there is a relation between these presumably embolic conditions and "Paget's quiet necrosis," which is discussed by Hindenach in this issue. Quiet necrosis may, it seems, be due to trauma with a superimposed low-grade staphylococcal infection, but its results are not unlike those due to infarction.

ARTHRITIS IN ANIMALS

THE professor of comparative pathology at the University of Pennsylvania has lately described [3] the lesions found in 777 specimens out of 1749 dried skeletons in a number of museums, as well as similar lesions in wet-cleaned bones examined during three years in the pathological service of the Zoological Gardens in Philadelphia. Even in wild animals he finds signs of arthritis corresponding to those seen in man. These, however, are confined to the larger animals, including apes, hyenas, bears, oxen, stags, and the cat tribe, and none have been observed in the dog tribe or in rodents or bats. Domestic animals are not included in this study, but it is known that draught horses, for example, often show arthritic changes in the joints.

Some skeletons of gorillas present lesions which correspond, in Prof. Fox's opinion, with "all varieties of arthritis" found in man. In the wild boar the larger bones show ridging, as if muscular insertions had pulled upon the periosteum and produced overgrowth. This is interpreted as a "senile periosteal overgrowth, possibly a tension or traumatic reaction." Four bears in the zoo were "not suspected of having such severe articular disease," and the same may be said of the joints impaired simply by overwork in some elderly men and women. An old grizzly had general hypertrophic arthritis, the anterior extremities being especially affected, with more advanced changes in the right metacarpals than in the left. Among the hyenas 9 out of 16 specimens had widespread lesions—"a very striking picture." In these animals there is great development of the anterior musculature and the lesions in the hind limbs were negligible. It should be noted that arthritis is *not* found in young menagerie animals, with which may be contrasted the high incidence of rheumatoid disease in early adult age in man.

Prof. Fox cites many facts which suggest a correlation between function and lesion, such as the hand and foot lesions common in primates and the liability to arthritis in the muscle-joint-combinations that bear the greatest strains, jolts or shocks. His radiograms and descriptions of animal lesions are typical of osteo-arthritis, a wear-and-tear disease of adult or later age, in which strain and traumatism and degenerative processes—often premature—play the chief part. It is widespread in the world and was perhaps as prevalent in early times as it is today. That it occurs in the larger animals, subject to the same causal influences, is a significant fact. On the other hand there is, we believe, little or no evidence that animals are affected by rheumatoid arthritis, now usually regarded as an infective and atrophic disease in which neither degenerative changes nor the influence of trauma can be traced.

2. Kahlstrom, Burton and Phemister, *Ibid*, March, 1939, p. 631.

3. Chronic Arthritis in Wild Mammals. By Herbert Fox, professor of comparative pathology, University of Pennsylvania. Philadelphia: The American Philosophical Society. 1939. Pp. 76. 9*s*.

BLOOD-LETTING FROM THE FEMORAL ARTERY

IN obese patients with falling blood-pressure and collapsed veins, blood-letting may sometimes be desirable but difficult. Greatly daring, as some may think, Émile-Weil [1] has devised an alternative method which he has found both simple and satisfactory. In cases where venesection is troublesome or impossible, he inserts a trocar, directing the point upwards, into the femoral artery, which even in the most collapsed patients is always easily identifiable by its pulsation. By this means it is possible, he claims, to withdraw any desired quantity of blood quickly and without risk of clotting or subsequent hæmorrhage. For the sake of convenience and tidiness he recommends that the blood be caught in a flat graduated basin. When enough blood has been let, the trocar is withdrawn and pressure is applied to the puncture for half a minute. This, aided by the elastic recoil of the arterial wall, seals the wound completely. Émile-Weil cannot see why the method should fail even in the most inexpert hands. It will perhaps commend itself to the courageous; though they may like at first to include a tourniquet in their arteriosection kit.

LIVERPOOL HOSPITAL SCHEME

As a preliminary step in launching a public appeal for funds to build a new voluntary hospital in Liverpool, Mr. A. V. J. Hinds, in a booklet entitled "Hospital Testament" (University Press of Liverpool, Hodder and Stoughton Ltd., 6*d*.) asks why so necessary a thing as hospital treatment should depend on charity. Why not a state hospital service? Granted the necessity of state hospitals, how can the continuance of voluntary hospitals be justified—much less a progressive or intensified activity? In Liverpool, he says, the voluntary hospitals are saving the municipal authorities an annual expenditure of over £150,000. In Great Britain there are 1000 voluntary hospitals with a combined income of over £17,000,000, over 40 per cent. of which comes from voluntary sources and relieves the community of an annual expenditure of over £7,000,000. The care of the sick is only one part of what a hospital service does for the community. The hospital is really the source of all private medical service—general practitioner, consultant, and specialist. Research in clinical medicine is non-productive without the hospital, because in a hospital alone can be collected a sufficiency of cases. The service provided by the hospital is thus threefold: curative, educational, and scientific. The lay committee of a voluntary hospital, it is argued, is independent, not swayed by political or bureaucratic motives, and is a guarantee that the best available persons will be selected for staff appointments, the selection actually being made for merit alone by professional colleagues and not decided solely by a political body or a lay administrator. This means that the "best brains" serve not only as healers of the sick in hospital but also as university teachers and leaders of research. In

1. Émile-Weil, P., *Bull. Soc. méd. Hôp. Paris*, May 29, 1939, p. 802.

other words, the voluntary hospitals guarantee an alert and enterprising medical profession.

In Liverpool the nine voluntary hospitals associated with the medical school of the university have about 1400 beds, whereas the municipal hospitals have about 3000. It is recognised that the municipal hospitals have come to stay, and the policy of the voluntary hospitals in Liverpool does not envisage any increase in the number of existing beds in the voluntary hospitals in that area. The voluntary hospitals serve a large area extending to north Wales and south-west Lancashire, whereas the municipal hospitals can deal only with patients from within the city boundaries. For over three years there has been in existence in Liverpool an Associated Voluntary Hospitals Board, which has attempted to unify the policy of the voluntary hospitals, and it works with the Municipal Hospitals Committee on the Liverpool Hospitals Joint Advisory Committee. The four general hospitals (the Royal, the Northern, the Southern, and the Stanley) were amalgamated in 1938 to form the Royal Liverpool United Hospital. They will have to be almost entirely rebuilt within the next twenty years; so it has been decided to substitute for them, close to the university, one general hospital with 850 beds, the total now spread among the four; to coördinate so far as possible the activities of the special hospitals in the system; and, when the time comes for rebuilding each special hospital, to try to relate it to the new hospital in some sort of hospital centre. The four existing sites would be adapted as outpatient and casualty departments to serve the different areas.

RADIOSENSITIVITY OF MELANOMA

RADIOSENSITIVITY is a term that is often misunderstood. To say that a malignant tumour is radiosensitive implies only that it shrinks under the influence of radium or X rays; this is a purely macroscopic phenomenon, and is by no means always accompanied by the disappearance of all viable malignant cells. This use of the word gives rise to the paradox that many of the most radiosensitive tumours recur at the primary site and kill the patient, for radiosensitivity and a high degree of malignancy often coexist. On the other hand, radioresistant tumours, though they are often among the least malignant, also kill their host because they do not respond to treatment. It is therefore clear that sensitivity and resistance need not be related to the final result and prognosis. There is a widespread belief that because melanomata are rarely if ever cured by radium or X rays they are therefore quite insensitive, but Ellis[1] has now shown that this is often not so, for he describes 12 cases in which the tumour regressed after irradiation. This is not to say (and Ellis does not say it) that this form of treatment is as promising in melanomata as in other tumours. Ellis records a series of 38 cases seen at the Sheffield radium centre in the years 1931–37. Excluding untreated cases and those in which an eye with a primary growth was removed, there remain 27 cases in which it is possible to attempt to assess the value of radium or X rays. Of these, 8 have lived for periods ranging from one to six years without recurrence. It is of course possible that in some of the others life was prolonged and recurrence delayed by the treatment; improvement as distinct from cure is difficult to estimate. The fact remains that less than 1 patient in 3 can have been cured. Thus, though it must now be accepted that some melanomata are certainly radiosensitive, it has yet to be proved that in these tumours irradiation is the treatment of choice.

1. Ellis, F., *Brit. J. Radiol.* June, 1939, p. 327.

FREDERICK HOBDAY

ON the evening of Oct. 24, 1923, Clifford Allbutt presided at a memorable occasion, of which the object was to celebrate the unity of medicine as a biological study. It was the first meeting at the Royal Society of Medicine of the section of comparative medicine. As physic was divorced from surgery and mind from body, so, said Allbutt, had medieval perversity separated diseases of animals from those of mankind.

[Harrods

We recall this occasion because it was the aim of Hobday's later life to bring the animal medicine in which he had been bred and born into fruitful relation with human medicine. He was the first veterinary president of the new section. And it was not merely the utilitarian side of the relation which interested him. He was particularly conversant with the diseases common to man and animals; his own work lay largely in that direction, and he had been highly successful in applying Listerian methods to veterinary surgery. But he was convinced of the place of veterinary science in the larger medicine, if only because the material of study, ranging over many general and even orders of the animal kingdom, was more broadly based than that of medicine, which observes a single species. It was this conviction which led him to devote the fund raised on his retirement to the inauguration of a chair of comparative medicine and of a doctorate open equally to graduates of the human and the veterinary branches of medicine. He had been invited by the Chadwick trustees to deliver a lecture on this theme which was to have been the crowning achievement of his life. All those who knew him as friend of man and animals might unite to ensure that his purpose is still achieved.

On his own ground too Sir Frederick Hobday deserved his popularity and success. Having qualified in 1892 at the Royal Veterinary College he began at once to teach there and soon made up his mind that veterinary medicine was not going to flourish in effete surroundings. What was good enough for St. Bel in 1790 was not good enough in 1900 for the chief centre in this country of veterinary teaching. Hobday soon showed that he could get things done, and, equally to the point, that he could persuade people to provide the necessary funds for doing them. He raised nearly £300,000 for the new buildings in Camden Town and remained principal until they were opened by Royalty. During the whole time he was principal of the college he was also president of the organisation devoted to animal welfare now known as U.F.A.W., which appealed to him as the embodiment of practical humaneness. He was indignant of cruelties to animals under whatever guise and helped to espouse measures to eliminate

needless suffering. From his earliest days he worked on the problem of anæsthetising animals and birds and it was his apparatus which first made it possible to administer chloroform safely to dogs. The elaborate chapter on the administration of anæsthetics in the recent fourth edition of his "Surgical Diseases of the Dog and Cat" is largely a record of his own effort. It has been said with some justice that Hobday thought not so much with his head as with his heart, but animal life may feel content with that kind of thinking.

A SIMPLE WAY OF KEEPING MILK

FRESH milk is a temperamental and unstable fluid, inclined to rapid and devastating loss of flavour, and many ways have been tried to prolong its life beyond the few hours which any but the cleanest milk will keep under average temperature conditions. Pasteurisation, sterilisation, "buddeisation" and the Hofius process are all used or have been used, but most of these methods require complicated and expensive apparatus. Now Davis [1] of the National Institute for Research in Dairying has described a surprisingly simple method that may prove of great value in conserving milk for days without the use of elaborate machinery. It consists in adjusting the pH of the fresh milk to 5·2 with dilute hydrochloric acid and maintaining it at between 36° and 38° F. In this way the milk may be kept for a fortnight or more—that is, three or four times as long as commercial cooled pasteurised milk will keep—and may then be brought back to its original pH before use by the addition of an equivalent amount of dilute caustic soda. The result is a milk that is said to retain its original flavour unchanged. So far the method seems to have been tried on only a small scale, but if it proves equally effective on a large scale it will have several obvious applications in the milk industry. It will remove one of the minor annoyances of ocean voyages of up to a fortnight's duration, it will simplify the adjustment of supply to demand over the week-end, and it will help the manufacturer of milk products to deal with a rush period when for a few days the inflow of milk may exceed the capacity of his machinery. In time of war, when delays in transport may be both unpredictable and unavoidable, it might be a convenient way of treating bulk milk carried in tanks by road or rail. Further information is needed as to the viability of the commoner pathogenic organisms in milk acidified in this way, and as to the possibilities of combining the method with pasteurisation. Various difficulties besides the mechanical one of adding acid and alkali to milk on a large scale may have to be overcome before commercial success is attained, and unfortunately legal considerations may also weigh heavily against the process, for it involves diluting the milk to the extent of some 8 per cent.

LOCAL EFFECTS OF ADRENALINE

THE inhalation of a vaporised solution of adrenaline as a treatment of bronchial asthma was introduced some four years ago and is now used extensively. The strength of the solution has been progressively increased from the original 1 per cent., and a 10 per cent. solution is now often prescribed. Galgiani and his colleagues [2] have lately investigated the local effects of these solutions on the pharyngeal and bronchial mucous membranes. By tracing the course of gentian violet vaporised in the mouth of a patient with a bronchial fistula they showed that most of the inhaled vapour is deposited on the pharynx, larynx and trachea, a finding that agrees with the conclusions of Spoto [3] and Rubow [4] that in dogs and rabbits not more than 3 per cent. of the inhaled vapour reaches the lung. They next showed that clinically the adrenaline deposited on the mucous membrane of the upper respiratory tract usually has no systemic effect, and they confirmed this fact in cats, but they found that the bronchial mucosa of cats absorbs adrenaline well, pulse and blood-pressure changes being demonstrable after the deposition in a bronchus of 0·0002 mg. To reach an equivalent concentration in the human bronchus by inhalation would, however, require something like a hundred inhalations. They concluded that the anti-asthmatic effect of the drug is due to its direct action on congested bronchial mucosa and spastic musculature, and not to its absorption into the general circulation.

The next part of their work dealt with the effects of long-continued use. They were able to show that repeated inhalations produce pharyngitis and tracheitis in animals, and that swallowing the solution causes gastro-intestinal changes. A man who died of pulmonary tuberculosis after having frequent inhalations of 1 per cent. adrenaline during the 48 hours before death also showed post-mortem signs of pharyngeal and tracheal irritation. Some time ago Fox [5] demonstrated the destructive effect on the respiratory mucous membrane of the prolonged application of adrenaline and ephedrine, and most laryngologists are familiar with the patient complaining of "nasal catarrh" who has used one of the proprietary preparations containing adrenaline, ephedrine or Benzedrine for a long time, and with the cure that results when it is discontinued. The conclusion is unavoidable that adrenaline and similar compounds are unsuitable as local applications to the upper respiratory tract except for brief periods, and that their repeated use in chronic disease is therapeutically unsound.

EXCRETION OF CALCIUM AND MAGNESIUM

THE impression is still widely held that the excretion of calcium and the heavy metals takes place largely through the gastro-intestinal tract. There is already doubt, however, as to the excretory function of the bowel in the case of iron, in fact the body seems to have little ability to excrete iron at all when once it has been absorbed, and lately doubt has also been thrown on the part played by the bowel in the excretion of calcium and magnesium. The calcium of the fæces can theoretically be regarded as made up of three fractions: (*a*) the unabsorbed calcium of the food, (*b*) the calcium secreted into the bowel in the digestive juices and not subsequently reabsorbed, and (*c*) the calcium excreted specifically direct into the bowel. McCance and Widdowson [6] have studied the excretion of calcium and magnesium in the form of gluconates after intravenous injection in normal people, and have found no evidence of specific excretion of the injected metal into the bowel: the injected calcium or magnesium was indeed excreted rapidly and nearly quantitatively, but the additional excretion took place almost entirely by way of the kidneys and there was no increase in the calcium or magnesium

1. Davis, J. G., *Nature, Lond.* June 17, 1939, p. 1025.
2. Galgiani, J. V., Proescher, F., Dock, W., and Tainter, M. L., *J. Amer. med. Ass.* May 13, 1939, p. 1929.
3. Spoto, P., *Arch. int. Pharmacodyn.* 1930, **39**, 263.
4. Rubow, V., *Hospitalstidende*, 1925, **68**, 169.
5. Fox, N., *Arch. Otolaryngol.* 1931, **13**, 73.
6. McCance, R. A., and Widdowson, E. M., *Biochem. J.* April, 1939, p. 253.

content of the fæces. The ratio of fæcal calcium or magnesium to the intake in the food was unchanged by intravenous injection of large quantities of the metal. It seems, therefore, that the intestine has little or no regulatory action in connexion with the excretion of calcium or magnesium, which is in agreement with the earlier results of Nicolaysen,[7] and that the calcium or magnesium of the fæces consists merely of that unabsorbed from the food together with that secreted in the digestive juices and not reabsorbed. This conception is easier to reconcile with clinical findings than the older view of a specific excretory function of the bowel, for the majority of diseases which lead to decalcification, such as hyperparathyroidism and hyperthyroidism, do so chiefly by increasing the urinary excretion of calcium, the fæcal calcium being usually little different from normal. Experimental procedures, such as the administration of parathormone or acidifying salts, also increase the urinary calcium without having any significant effect on the fæcal excretion. The only conditions in which the fæcal calcium is appreciably raised are those such as steatorrhœa, where the effect is much more likely to be due to interference with absorption than to normal absorption and excessive intestinal re-excretion.

Surgeon Captain J. A. MAXWELL, O.B.E., F.R.C.S.E., who accompanied the King and Queen on their voyage to America and back, has been created a commander of the Royal Victorian Order.

The British Hospitals Association has appointed a war emergency committee to consider what part the voluntary hospitals should play in the scheme of hospital services in the event of war. The proposal arises from the belief that adaptation and organisation are essential if the voluntary hospitals are efficiently to perform the service which would be expected of them in a national emergency. The committee consists for the most part of lay officers of hospitals in London and thirteen other large towns, but in three cases a medical man has been nominated by the hospital: Mr. Harold Collinson (Leeds), Prof. T. B. Johnston (Guy's), and Mr. C. Max Page (St. Thomas's). Mr. O. N. Chadwyck-Healey is chairman of the committee and its secretary is Mr. A. G. L. Ives (address 12, Grosvenor Crescent, S.W.1.).

FIRST-AID AT ST. MARYLEBONE

THE borough of St. Marylebone staged a demonstration of the work of stretcher parties and a mobile first-aid post on June 21. Some houses undergoing demolition were used, and the onlookers and the mobile first-aid post were placed in an adjacent plot of waste ground. It was assumed that the houses had been damaged by a high-explosive bomb, the warning had been given, and the rescue-parties had released the people under the wreckage. The exercise began with the arrival of the stretcher-party combine, consisting of the stretcher party in its car, an ambulance, and a car to carry sitting casualties. Along with the combine came the mobile first-aid post in a lorry. Immediately on arrival the stretcher-party combine started work, and it became apparent why the various units must be considered as a combine and not as having little connexion with each other. In this case the work of the stretcher party and the ambulance crew dovetailed without a hitch, but it was easy to see the kind of confusion that would arise if coöperation was not carefully prepared.

While the stretcher-party men were administering simple first-aid and bringing out the casualties, the mobile first-aid post was being unloaded from its lorry and set up for work in the open. Standard equipment was carried, and a staff of one doctor, six nurses, and two male attendants. Ministry of Health regulations do not allow any male attendants for a mobile first-aid post, but the exercise demonstrated clearly that they are needed. Casualties were then helped or carried from the houses and disposed of: the gravely injured by ambulance to the nearest hospital, and those whose injuries were such they they could wait for full surgical attention to the first-aid post. The trivially injured also were taken to the post, and it was explained that some of these could be discharged without further attention at the hospital.

It was seen that the mobile first-aid post acted as a screen for the hospital and prevented it from being crowded with the full number of casualties, although the importance of this could not fully be demonstrated on such a small scale, with only about a dozen casualties. In reality, as is taught at the Home Office A.R.P. staff school, it is unlikely that raids would consist of widely scattered bombs; bombs would fall in groups or "patterns," the full load of a squadron of aeroplanes (about 9 tons) being dropped in one small area.

This concentration of the attack would have many important effects. The number of casualties in the damaged area would be large; figures for the late war and for the Spanish war point to something like 75–100 casualties per ton of high explosive. It was noticeable that the mobile post was only able to deal with two or three stretcher cases and five or six walking cases in about three-quarters of an hour, despite the fact that the work was mere demonstration and not actual surgery. In war very large numbers would have to be dealt with, and moreover, if Spanish figures are to be trusted, only 15 per cent. of these would be walking cases. Before he could start work, therefore, the doctor would have to spend a good deal of time inspecting the casualties and deciding which should be attended to first. If the mobile post were working in close contact with the stretcher party in the damaged area, there is little doubt that he would also be called on to decide which casualties should go direct to the hospital and which should be attended to at the post. This would mean that there would be a considerable delay before he could start any actual surgery. It therefore seems that there should be another doctor on the spot to classify casualties, or all casualties should be taken as quickly as possible to a post arranged to deal with the full number.[1]

Here the post was set up in the open and not in some convenient building. This presumably was done for demonstration purposes, so that the work could more easily be seen. Yet in actual war conditions the strictly limited protection of an ordinary building would be little comfort to casualties who had so recently experienced the effect of high-explosive bombs on similar structures. It is to be hoped that the recommendation of the Hailey report that such work should be done in full shelter is soon to be carried into effect.

7. Nicolaysen, R., *Skand. Arch. Physiol.* 1934, **69** (suppl.) 1.

1. See Crome, L., Fisher, R. E. W., and Shirlaw, G. B., *Lancet*, March 18, 1939, p. 655.

SPECIAL ARTICLES

IMPERIAL CANCER RESEARCH FUND

OPENING OF NEW LABORATORIES

ON June 27 Sir Humphry Rolleston deputised for Viscount Halifax, the president of the Imperial Cancer Research Fund, in formally opening the Fund's new laboratories at Burton Hole Lane, Mill Hill. The laboratories were moved to Mill Hill from Queen Square a year ago and have been in use since last July. The choice of site was determined by the decision of the Medical Research Council to build their Central Institute at Mill Hill, for it was felt that the small and highly specialised staff of the fund would benefit by direct contact with colleagues with interests in other fields. The new buildings provide facilities that are far in advance of any that the fund's staff have enjoyed hitherto.

SIR GOWLAND HOPKINS'S ADDRESS

At the opening ceremony Sir Gowland Hopkins spoke on the importance of laboratory effort in cancer research. "I have spent much of my life in laboratories," he said, "and it has been one of my main interests to try to follow the effect of that great increase in the number of laboratory workers which has occurred in my time, not only in this country's contribution to scientific knowledge as a whole, but to medical progress in particular." He recalled the time when accommodation and opportunities for experimental research were sadly to seek in this country. It was then the almost universal custom among young men who hoped to devote some of their energy to scientific research to spend an apprentice year or two abroad, usually in a German laboratory, where inspiration and adequate equipment might in those days be most easily found. For this expatriation, he said, there is happily no need today, but the provision of still more laboratory accommodation would benefit both science and the country. Increases in the accommodation provided for skilled laboratory effort have never failed to be justified by results. In growing science the Law of Diminishing Returns finds no application. Our knowledge of nature has grown great, but the extent of our ignorance is much greater.

THE EXPERIMENTAL METHOD

In emphasising the extreme importance of laboratory activities in the world-wide endeavour to solve the problems of cancer, Sir Gowland Hopkins hoped that he would not be thought to be undervaluing the knowledge won by other means, or the skill with which existing knowledge is applied by those whose immediate task is to relieve suffering. Of the more recondite aspects of the cancer problem the lay public usually know but little, and there are many who fail to recognise the importance of their study. Yet it is most unlikely that a complete mastery of cancer will arrive until we reach to fuller knowledge of its intimate nature as a phenomenon of uncontrolled growth. But knowledge of this kind must be sought deeper down in the nature of things than can be reached by observation alone, or by any superficial method of study. While the cure of cancer must become ultimately a medical problem, to discover its fundamental nature is a biological problem of great complexity. We are at least not likely to reach any solution of this without sustained efforts based on experimental methods. These in particular are the task of the laboratory.

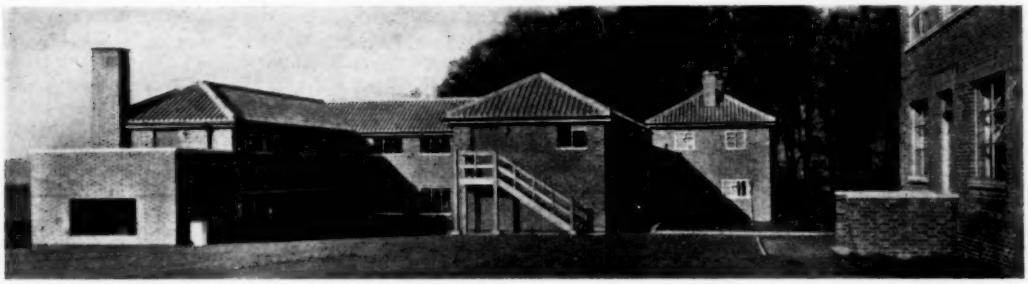
Of the many possible illustrations of the special advantages of the method of experiment Sir Gowland Hopkins chose the establishment of the distinction between typhus and typhoid fever. William Jenner compared side by side every characteristic of the two diseases which could be observed and recorded, and this in a great number of cases. In sum, the evidence as one reads it today seems not far from being conclusive. But each individual item contained in the evidence lacked constancy; each contributory argument could be criticised, and was criticised, by many. Complete conviction did not come. Meanwhile, Pasteur the experimentalist was at work. Only a few years had to elapse before his brilliant and carefully controlled experiments had established, once for all, the microbic origin of infective diseases. It was still some years before the exact nature of the specific agents responsible for typhoid and typhus fever could be described, but this was merely a question of developing technique. Such evidence was bound to come after Pasteur had once started the right lines for thought and method. Real progress, and even important generalisations may doubtless result from the recording of systematic observations on aspects of phenomena directly revealed to the senses and in the established conditions of ordinary experience. In cancer research morphological studies have yielded indispensable information but they could throw little light on the underlying phenomenon of morbid growth. It is characteristic of the experimental approach to phenomena that it often yields knowledge of a kind quite unforeseen. The unknown aspects of nature that it reveals are of course part of reality, and only remain unknown because in our customary contacts with nature the conditions which reveal them to our senses are not established. The experimentalist chooses his own conditions.

Many people are inclined to say "we know that the experimental method has created subjects like modern chemistry and physics, but do not the problems of cancer belong to a category quite different from that which included subjects such as these?" We are sure today however that, like so many other biological problems, those of cancer are closely interwoven with those of the fundamental sciences.

Some years ago it used to be said that we shall never fully understand the manifestations of cancer until we have solved the riddle of life itself, with the implication that this will always remain unsolved. Such a view needs much qualification. At one level at least of their organisation living tissues are essentially physical and chemical systems, and it is at this level we must expect to find a basis for the differences displayed by cancer cells and normal cells. If the material basis of life has esoteric qualities which are neither physical nor chemical, these will not intrude into this particular arena.

EARLY WORK ON CANCER

The Imperial Cancer Research Fund was founded, Sir Gowland Hopkins went on, at a time when extreme confusion and pessimism prevailed in the medical profession on the subject of cancer. It was held, for instance, by most to be a constitutional disease due to obscure qualities in the make-up of individuals which involved a liability to the disease from which



The animal house. The building accommodates rabbits, guineapigs, chickens, fish and dogs, and contains two small laboratories. Larger animals such as sheep, pigs and goats live in houses in the meadow to the north-west of this building.

there could be no escape. Yet not a few believed it to be an infective and even a contagious disease inherent in civilisation itself. The highly civilised communities, owing to luxury and artificial habits in matters of food, drink and the like, were supposed to have acquired a liability not suffered by primitive races or by wild animals which live more in accord with the demands of nature. These and other dogmas current a generation ago, while inconsistent among themselves, were all of a kind to make the situation seem hopeless in respect both of the prevention and cure of the malady. The belief moreover that animals do not suffer from it was for would-be students of cancer most discouraging, because in the case of maladies suffered by both man and animals so much had been learnt for the benefit of the former by studies carried out on the latter.

The earlier years of this century saw the beginning of devoted efforts which have now replaced inhibitory dogmas by illuminating facts, and the outlook has changed and greatly brightened. The belief that cancer arises only in civilised communities was fated to disappear entirely as soon as more extended inquiries had proved its frequent occurrence in primitive races. That animals are liable to cancer had, as a matter of fact, been demonstrated before the end of the last century, and further confirmed early in this. The highly significant fact had also been established that if a few cells from a tumour arising spontaneously in an animal were transferred to the body of another of the same species they will there continue to grow and divide, thus producing a tumour in their new host in all respects similar to that from which they were derived. The significance of these facts was at first not generally grasped and the evidence was received with apathy and disbelief. Yet the modern and really progressive phase of cancer research began with a recognition of their significance, and the earliest work supported by the Imperial Fund greatly helped to initiate this progressive phase. The foundation of the fund in 1902 was indeed most timely; and, fortunately, its original staff was fully alert to the extreme importance of tumours shown to be transmissible, as illustrating one aspect at least of the essential nature of cancer. Its first director of research, Dr. E. F. Bashford, recognised clearly that so long as the study of its incidence was restricted to its incidence in civilised man progress must at best be very slow, and, in fundamentals, perhaps impossible. Investigations therefore had to be placed on a broad basis of comparative, statistical, and experimental studies.

Dr. Bashford contributed much to the proper interpretation of the available statistical data, and the fund has maintained its interest in this side of research; it possesses today a very expert statistical subcommittee. The main activities of the fund's laboratories in the first years were devoted to a thorough and enlightened study of transmissible cancers. With increasing experience spontaneous tumours of various types were found to be by no means uncommon in animals, and they occurred in a variety of vertebrate species. When a few cells from any one of these growths were transferred to another animal of the same species their growth continued, forming in the new host, as the much more limited earlier experiments had suggested, a tumour identical with that from which the cells originated. It was also established that the implanted cells did not induce malignant growth in the normal cells surrounding them. The tumour was formed from their own progeny alone. These facts illustrate a fundamental aspect of the nature of cancer, and their establishment at once gave a more hopeful outlook

The main laboratories. In ground plan the institute is shaped like the letter T. The wing to the left is used exclusively for animals under experiment. The library, office, workshops, staff tea-room and store-rooms are on the ground floor, while the laboratories, operating-theatre, &c., are on the first and second floors.

for the surgeon's art. Cancer was shown to have local origins, and not to be a constitutional disease. That is why the removal of a growth at a sufficiently early age may completely eradicate the disease.

The conviction grew that malignant cells possess everywhere the same fundamental properties, and this is the foundation on which the experimental investigations of cancer, as it exists today, is built. Of the diseases which can be produced experimentally few, if any, simulate the human disease so closely as cancer. The laboratory of the fund, directed after Dr. Bashford's death by Dr. J. A. Murray, did more than any other centre at that time to establish these important aspects of knowledge. The fund's staff were pioneers in this country in the systematic study of cancer by experimental means. Since they began their labours centres for cancer research have greatly increased in numbers, and are to be found in nearly every civilised country. It was twenty years after the foundation of the fund that the British Empire Cancer Campaign began to administer the large endowment for research which its appeals to a generous public have provided. There is abundant room today for the widespread activities of the Campaign and for the independent efforts of the Imperial Fund.

The library.

TREND OF RESEARCH TODAY

In 1911 Dr. Peyton Rous of the Rockefeller Institute in New York described a form of cancer in the domestic fowl which could be propagated not only by grafts of its cells but by cell-free filtrates made from them. A small quantity of such a filtrate from a tumour present in one bird, when injected into another, produces a growth exactly similar to that from which it originated. Thus was revealed a pathogenic agent then new to the field of cancer research. This discovery has led to a multitude of important studies in which Dr. Gye has played an important part. It was at first thought by many that the growths yielding these active filtrates were not true cancers, but the supposed distinction has since lost its significance. Cumulative evidence has brought conviction that the pathogenic agent in such filtrates is a virus. It belongs therefore to a class of agents now well known as being the effective cause of various diseases in man, animals and plants. Characteristic of viruses is their ability to multiply in the body of the infected host, but unlike bacteria they do so only as tenants of living cells.

A corner of one of the research laboratories. Large windows like this one are provided throughout. The benches are supported by the cantilever system.

In a great number of cases at least, he said, we have to recognise in the file of cancer causation the initial influence of an external agent which, acting from the environment, may cause normal tissue cells to become cancerous. Such may perhaps be called provocative factors in the field of causation. When one of them has acted for a sufficient time, which fortunately is usually a very long time, tissue cells previously exercising only their proper physiological functions may be led to grow pathologically. The influence of many of these external factors has long been recognised. Long contact with certain chemical substances is one of them, as in the so-called occupational cancers. Workmen liable to continued contact with shale-oil products, with tar or soot, and more rarely with arsenic, aniline and some other substances are prone to develop cancer. Long-continued mechanical irritation may induce it and also long exposure to certain forms of radiation, as was shown by the sufferings of those who worked with X rays and radium before their power to produce cancer was known.

Such causative influences are exerted most readily on the skin and superficial parts of the body, and their effects are there easy to observe. It is quite possible however that provocative factors, doubtless differing in kind from these, are concerned in initiating growths elsewhere in the body. Such effects are apt to be spoken of as being due to prolonged "irritation," but irritation is a word with vague meanings, and we have to learn why only in certain circumstances does irritation become a stimulant to growth. To attain a more definite understanding of the phenomena involved we must study the nature of internal events in tissue cells which pass from quiescence to active growth. It is necessary, for instance, to discover whether the growth provoked by an external agent is always associated with chemical or physical changes in the internal economy of the cells, and, if so, to learn what is their precise nature. If constitutional changes must exist before growth can begin, we should look on their establishment as involving

links in a chain of events of which morbid growth is the final outcome. But certain alternatives arise here for consideration. Do external factors supply only an initial impulse to growth, which once started continues without their continued influence? This must be true of such environmental factors as chemical or mechanical irritation and radiation. On the other hand, in the case of a concrete agent such as a virus its continued presence may be necessary as a stimulus for the continuance of growth. At the same time when growth begins apparently as the direct result of "irritation" of any kind, it may be that the real effect of this is merely to reduce the cells' resistance to the entry of such an agent as a virus. Again, it is possible though not probable that the modifications which lead to growth may in some cases occur spontaneously, as a mutation in the metabolism of normal cells.

Considerations of this kind are guiding current researches, and knowledge today is fast increasing, not in extent alone but also in precision and significance. As an instance in justification of this claim Sir Gowland Hopkins mentioned the brilliant experimental work during the last few years based on the long-known fact that tar can induce cancerous growths. The combined efforts of the pathologist and organic chemist have shown that it is certain specific substances in tar which are alone responsible for the effects. The exact constitution of these substances is known, while others related to them have been artificially synthesised, and their graded capacity for inducing cancer carefully determined. These cancer-producing substances, though differing from them in details, are akin chemically to substances natural to the body—for instance, to the hormones which control certain of the functions of sex. Indeed it has been shown that in experimental animals subjection to prolonged administration of a sex hormone encourages the growth of glandular cancer, especially cancer of the breast. On the other hand work done in the laboratory of the fund has shown that by the simultaneous administration of yet another hormone this result can be prevented. Such objective facts as these should encourage equally objective and sane thought about a malady which has been so often viewed in the past from a standpoint which was almost that of superstition.

Workers in a centre of experimental activity devoted wholly to one limited end may be in danger, owing to their special preoccupations, of ignoring too much the advances won in other branches of scientific endeavour. These may often contain suggestions and even inspiration which can contribute greatly to the progress of their special task. Frontal attacks alone are proverbially not always the most successful method of dealing with an entrenched enemy. In cancer research this is especially true. Here workers should have liberty and leisure to pursue paths which, though apparently remote from what seems to be the direct one, may prove to be short cuts towards that goal.

In conclusion Sir Gowland Hopkins briefly appraised the present position of the cancer problem and maintained that it shows reasons for much satisfaction.

With the assurance that fundamental knowledge concerning the actual nature of cancer is continuously increasing, together with the realisation that success in treatment grows with the clinician's increasing skill and equipment, there is surely justification today for an optimistic outlook. It is most desirable, he said, that the lay public should be persuaded to share in such optimism.

JUVENILE AND ADULT CRIME

JOINT CONFERENCE ON DELINQUENCY

THE Magistrates' Association initiated an important step in the scientific study of delinquency by calling a conference, with the coöperation of the British Medical Association, at B.M.A. House on June 23. The object of the conference was to discuss how medical and psychological knowledge could be made available to magistrates in their duties, both in court and elsewhere. The morning session dealt with juvenile and the afternoon with adult crime.

THE MEDICAL OFFICER IN THE JUVENILE COURT

Lord ALNESS presided over the morning session, and after his opening remarks Miss MADELEINE SYMONS, J.P., president of the Stamford House Juvenile Court, spoke. Magistrates sitting in the juvenile court, she said, cannot do their work without the help of the medical psychiatrist at the remand home, and of the child-guidance clinics, hospitals and individual doctors who examine children on bail. The practice of remanding for a purely medical examination is growing, but it is necessary to bring home to magistrates the necessity for a simple physical examination in many cases, or otherwise epilepsy, bad eyesight, pregnancy and gross mental deficiency may go undetected. The psychiatric help given to London courts is common sense applied by trained people. The root of the problem is financial: not enough money is spent on remand homes, and for the examination of children on bail the courts have been sponging on the generosity of doctors and charitable organisations. Outside London many courts have no funds to pay for the examination of children on bail. Some of the difficulties, she said, could be smoothed out by clauses 19 and 38 of the Criminal Justice Bill if it becomes law, but a serious omission from the bill is financial provision for the medical examination and treatment of children who are not offenders but who require care and protection, or are beyond control. Adequate medical facilities are also lacking; the passing of the bill into law may stimulate their provision, but a mushroom growth would be undesirable. She hoped that the new act will help in the extension of boarding-out. The vital decision whether the courts want a full physical examination or a report from a psychiatrist in a particular case rests in the hands of lay magistrates. They can only make this decision wisely if with medical help they train themselves to choose the cases which need treatment, and if they can rely on reports from properly trained probation officers who have plenty of time. Miss Symons urged that they should use fully their existing powers of remand.

INDICATIONS FOR SPECIAL MEDICAL EXAMINATION

Dr. WILLIAM MOODIE admitted that his remarks would probably be distressing, disturbing and somewhat destructive. A doctor present in court, he said, can give very little help in selecting cases. He cannot pry into a child's soul on the spot and can only detect gross abnormality. He cannot advise the court unless he has a considerable amount of information about the child. Reference for medical examination has in view the best disposal of the child: treatment is far more environmental than personal. The psychiatrist must estimate the intelligence, allowing for "verbal fluency," and decide how far the child is responsible. Delinquents are on the whole, through their hostility

to the world, more backward than other children and do less well in school, so the degree of the child's hostility must be estimated. Without all this and other information about the child and his circumstances, no doctor is justified even in advising the court.

OBSERVATION, DIAGNOSIS AND REPORTS

Dr. J. D. W. PEARCE, in dealing with reports on patients in custody, said that remand for special report is no handicap to the examination but rather facilitates it. Remand homes are planned primarily for non-delinquents; the remanded child attends ordinary school classes and takes part in physical drill, games and entertainments; he settles down as at home. In the absence of a history Dr. Pearce's custom is to state the material on which he makes his report. In his opinion for nearly all cases the examining doctor should be a man, as the delinquents are mostly boys and the girls are usually older and will confide more easily in a man. A stripped examination is essential, or important physical disabilities may be missed. The doctor must be in touch with general medicine, familiar with academic psychology and trained in psychiatry, and must be able to mix with patients on the common ground of humanity. He should follow a strict routine. His report must be short, lucid, unambiguous, simple and definite, and he must frankly disclose its deficiencies. He is at liberty to ask for a further remand if he thinks it necessary. Dr. Pearce urged that more child-guidance clinics should be established throughout the community; they are the most suitable agencies to do the reporting for the courts.

TREATMENT

Dr. DENIS CARROLL pointed out that the word treatment includes any method of disposing of an offender which a psychiatrist may prescribe. The object must be borne in mind at every stage, and the causes, which are multiple, must all be taken into account. They call for several simultaneous and sometimes contradictory methods of treatment, and the psychiatrist must strike a balance. On the penal side of treatment a doctor rarely has anything to do, but may sometimes advise. Sociological treatment includes Borstal, approved schools, short periods in remand homes, camps, hostels and different kinds of work. Medical treatment must be directed towards organic disease, and the court must use its influence to see that parents facilitate the treatment. Psychological treatment includes suggestion, persuasion and re-education, and sometimes analytical methods. Probation officers who have attended courses on these methods and their aims are doing better work. Superficial causes can be dealt with by psychological and sociological measures, but the deep causes need medical advice and usually also medical attention before the actual treatment.

Prognosis, Dr. Carroll went on, depends partly on age. The younger the offender the better the outlook, but the habit of crime may be a more important factor than the age. The outlook also depends on how bad the mental state is in relation to the delinquency, on defects in the environment, and on the friendliness or hostility of the offender to the people who deal with him. The degree of coöperation he will give can be estimated by practical methods. The Criminal Justice Bill contains the valuable provision that medical treatment may be ordered at any time within three months after the making of the probation order. If this is enacted the doctor will have adequate time to come to a decision. Magistrates and probation officers should receive instruction from the medical angle, for they must form part of a team with the psychiatrist, the psychologist and the social worker. A routine remand in custody is unnecessary and expensive. Most of the children can be dealt with in an outpatient clinic —any psychiatric outpatient department of a general hospital with a children's branch or any child-guidance clinic. A court or doctor in doubt where to send a child should write to any clinic in the district, the Child Guidance Council, or the Institute for the Scientific Treatment of Delinquency. Dr. Carroll hoped that the powers proposed to be given by the bill to local authorities to subscribe to voluntary bodies maintaining observation homes or hostels for delinquents will be used if they become law, and that magistrates will press the authorities to provide such inpatient accommodation. If enough cases are referred by the courts, facilities will be forthcoming. The limitation of treatment on a court order to twelve months is bad, and the treatment of some residential cases will collapse if payment is stopped at the end of that time.

DISCUSSION

Several speakers suggested that both male and female doctors should be available for examining delinquents. Mrs. E. G. F. BIRLEY (Manchester) thought that only a woman doctor should examine physically assaulted children, and Dr. HELEN BOYLE remarked that some boys respond more readily to a woman doctor. Dr. PEARCE, however, reminded the conference that few authorities would appoint two examiners, on the ground of expense, and only a small minority need a woman doctor exclusively. Mr. CLAUD MULLINS urged the need for punishment coupled with treatment, and declared that the probation system has been damaged by the exclusion of punishment. A fine may have value in a case where psychological treatment is needed. Dr. CARROLL agreed, with the proviso that treatment will be stultified if the offender is allowed to connect the punishment with it. Dr. R. F. BARBOUR stressed the need for examination in neutral surroundings after two or three days, so that the offender may have time to calm down; the examiner, he said, should see both parents.

Several speakers remarked on the legal difficulty of giving full information to the court before trial, particularly when it contains a statement of previous undetected offences. Dr. CARROLL said that some courts demand that all the information should be given in evidence in front of the offender, but much of the psychiatric information would be very undesirable for him to hear. Severe official comment has been made whenever the contents of reports have been disclosed to the offender, but the critics also apparently demand that the information should be given in the witness-box. Mr. ALBERT LIECK (London) said that all relevant information is admissible in the report and that anything adverse to the parents is required by law to be communicated. Miss SYMONS pointed to the statutory rule that the child or parent must be told the substance of such information as relates to the manner in which he is to be dealt with. Magistrates, she thought, should be educated to recognise the kind of information which does harm if communicated to the offender. Mr. MULLINS suggested the possibility of that rule and others being declared ultra vires by the High Court if they were challenged, and no speaker was able to suggest a solution of the difficulty. The medical requirement that the court should have full information on all aspects of the offender's life appears to conflict with the principle

of law that nothing adverse to an accused person should be made known to the court unless he is given an opportunity to rebut it by cross-examination and by evidence on his own behalf.

ADULT CRIME

In the afternoon session Mr. GEORGE A. BRYSON (Birmingham), who took the chair, agreed with Mr. Mullins's suggestion of the morning that probation without punishment is beginning to wear thin. He said that the problem of deciding which adults are suitable for treatment is even more difficult than that of selecting juvenile cases.

Mr. F. J. O. CODDINGTON, LL.D. (stipendiary magistrate, Bradford), said that the offender who comes before assizes for a serious crime is often remote from the ordinary run of humanity, and he deprecated the cheerfulness with which doctors are apt to report that such persons are not suitable for treatment. The adult offender with whom the petty-sessional court has to deal day in and day out, and who makes up the large majority of all adult offenders, is hardly distinguishable from the adult who does not come to court. The charges are nearly all concerned with petty theft, minor sexual offences and motoring offences. A large proportion of the accused are first offenders and ordinary, decent people; most of them could be saved from further crime. Mr. Coddington said that he sends to prison people he cannot deal with otherwise, and imposes fines in cases where they may be reformatory, especially if payment by instalments is ordered. Medical treatment is chiefly required for elderly first offenders, and for people whose offence is utterly unrelated to their position in life or apparently purposeless. The great variety of ill health and maladjustment in such persons is surprising. Important factors are change of life, pregnancy, epilepsy, arteriosclerosis, general ill health, partial deafness or blindness, and the fear of a strict husband combined with money worries. Many women offenders are utterly stale and a holiday works something like a miracle. Sexual maladjustment and loneliness are common factors.

Treatment by medical means, membership of clubs, a talk by the magistrate to the husband, arrangement for the gradual payment of debts, instruction in the elements of sexual hygiene, and similar common-sense measures are, in Mr. Coddington's experience, often successful. Petty sexual offenders he nearly always refers to the doctor, and is always able to bind over. They are often lonely old men who sometimes suffer from hydrocele or prostatic enlargement, and are reformed by the provision of companionship, the friendship of the probation officer or medical treatment. Young men are often restored to normality by the simplest psychological means: reassurance and an indication of a healthier outlook and way of life. Some doctors are incapable of appreciating the requirements of the magistrates, but most of them can be taught. The courts want a medical examination followed by a common-sense discussion from the psychological—not the psycho-analytical—point of view. Treatment, he maintained, should be planned from the medical and not the theological aspect. Delinquents respond to the fact that they are being treated medically and not punitively.

Prof. F. W. EURICH, to whom Mr. Coddington paid a warm tribute as his medical ally for many years in dealing with delinquents, said that an offender's obstructiveness soon disappears when he finds that the doctor has nothing to do with the criminal proceedings and that the magistrate only desires to help him. The doctor must study man as a whole and not confine himself to the psychological, or even to the medical, angle. Several obscure ailments may cause delinquency—e.g., hypoglycæmia, a thyroid growth, or constipation of organic origin. Apparent drunkenness in charge of a car may well be due to mild carbon-monoxide poisoning.

THE MEDICAL PSYCHOLOGIST AND THE COURT

Dr. J. R. REES put forward a classification of mental abnormalities connected with delinquency. He said that investigation by the Tavistock Clinic has shown that over half its adult cases are free from crime after three years. Reaction character traits are the hardest conditions to alleviate, and the psycho-neurotic delinquencies, inconsistent with the offender's ordinary culture and training, have the most hopeful prognosis. He suggested that a good beginning would be to encourage every court to send for psychological help all people who commit sexual offences or irrational acts, or who repeat offences. Fewer facilities are available for treating adult than child delinquents, but local-authority clinics will improve rapidly. Intuitive diagnosis is untrustworthy unless founded on a long practical experience of psychopathology. Expansion must be slow, and for some time the courts will have to be content with sound diagnosis and advice on treatment. A full treatment service is costly and cannot be organised quickly. The court should institute follow-up investigation for research into the value of treatment.

In discussing the afternoon's papers, Mr. MULLINS pointed to the grave difficulty that, outside London and the big cities, most delinquents are sentenced within a few minutes of the ascertainment of their guilt, and a remand for inquiry is unusual. Assizes and quarter sessions can only adjourn the case to their next sitting, which may be months in the future. Public opinion and the authorities must have impressed on them the need of time for proper inquiry between verdict and sentence. Only medical men can bring this need home. Dr. REES, on being asked what provision is being made for the training of medical officers for outpatient clinics in the country, said that the Institute for the Scientific Treatment of Delinquency holds week-end courses and lectures; the Tavistock Clinic gives two-year and shorter courses for psychotherapists; and the Maudsley Hospital provides lectures for the diagnosis but not the treatment of delinquency. If the new act results in enough remunerative work being available for these officers, he said that a supply will soon be forthcoming—especially if, at the same time, steps are taken to encourage young medical practitioners to take up psychotherapy in the provinces. At present no great inducement is offered to the newly qualified person to train in psychotherapy.

The conference resolved to recommend to the Magistrates' Association and the B.M.A. that a small joint standing committee should be established to further the coöperation of magistrates and doctors in the treatment of delinquency.

ELECTRONIC REACTIONS AND DIPHTHERIA.—The adjourned inquest at Leigh, Lancashire, on the boy who died from diphtheria after having been attended by Mr. C. C. Abbott, an unqualified practitioner who made his diagnoses on electronic reactions, was concluded on June 21 (see *Lancet*, June 24, p. 1457). After an absence of an hour the jury returned a verdict of death by misadventure.

THE LISTER INSTITUTE

CLINICIANS reading the whole of this year's annual report from the Lister Institute of Preventive Medicine will find themselves travelling far from the bedside. Sometimes it is the distant journey—the apparently remote investigation—that discovers the biggest treasure, whether for the cure or the prevention of disease. In a brief review of the year's work, however, we can mention only those of the institute's inquiries that have an immediate bearing on medicine or health; and, indeed, only a few of these.

VIRUSES

Acute rheumatism and rheumatoid arthritis.—Dr. G. H. Eagles has continued his studies on the ætiology of rheumatic infections. Attempts to demonstrate the infective power of the virus-like particles procurable by high-speed centrifugation of exudates and tissues from rheumatic patients have failed. In collaboration with Dr. W. H. Bradley, however, he has demonstrated that the sera of patients with rheumatic fever, rheumatoid arthritis and certain other arthropathies agglutinate such particles, whereas sera from persons in normal health do not. No consistent relation of agglutination to clinical phases was found, nor any evidence that it runs parallel to antistreptolysin titre or erythrocyte-sedimentation rate.

Acute rheumatism and the pleuropneumonia group of organisms.—Homer Swift and Brown, of the Rockefeller Institute, have recently announced the isolation of a pleuropneumonia-like organism from rheumatic-fever exudates (see *Lancet*, April 22, 1939, p. 938), and this may prove to be the long-sought ætiological agent of acute rheumatism. In any case the finding opens up a new field and already Dr. Eagles and Dr. Helga Jahn are collaborating with Miss E. Klieneberger, Ph.D., in the cultural study of rheumatic material. Should organisms of this group be recovered steps will be taken to determine whether the "virus bodies" studied at the institute by Dr. C. R. Amies and Dr. Eagles, which are agglutinated in the presence of sera from rheumatic fever and rheumatoid arthritis, are really the filtrable elements of a pleuropneumonia-like organism, or possibly breakdown products antigenically related to such organism.

Avian sarcoma.—Dr. Amies and Mr. J. G. Carr, working on the filtrable agents of the Rous I and other fowl sarcomas, report that it has lately become possible to obtain adequate amounts of these agents in a relatively pure form—i.e., in suspensions containing 1,000,000 tumour-producing doses per c.cm. Serological experiments with these concentrated suspensions have yielded still more evidence that the agent is closely related antigenically to some constituent of normal fowl cells. It has been established, for example, that the serum of a rabbit hyperimmunised with normal fowl protein will neutralise the tumour agent in vitro, and that these inhibiting properties can be removed by absorption with a concentrated suspension of the tumour agent. In the fowl, the agent behaves as a foreign protein because its presence in the malignant tissue and elsewhere elicits the formation of neutralising antibodies and agglutinins. It is believed that a full understanding of this phenomenon would constitute a big advance.

Smallpox vaccination with elementary-body suspensions.—In coöperation with Dr. R. G. Henderson and other officers of the London County Council, Dr. D. McClean (Elstree) has continued the experimental immunisation of nurses and children by intradermal injection of elementary-body suspensions of vaccinia virus. The resulting immunity, as tested by revaccination with Government lymph after not less than six weeks, has proved disappointing, and there is some indication that the development of a firm immunity depends on the development of a typical vaccinial vesicle at the primary vaccination. When applied by scarification, the suspension of elementary bodies produces typical vaccinial vesicles with general constitutional reactions indistinguishable from those produced by vaccine lymph.

SEROLOGICAL STUDIES

Antityphoid serum.—Mr. A. Felix, D.Sc., with the assistance of Miss R. M. Pitt has continued his investigations on methods of titrating therapeutic antityphoid serum. The Vi titres of the sera, as determined by the agglutination reaction, run parallel with their protective values as determined by tests in mice which received a test dose of living virulent typhoid bacilli. The O titres of the sera, as estimated by the agglutination reaction, run parallel with their protective values as determined by neutralisation tests in mice which received a lethal dose of killed typhoid bacilli ("endotoxin"). Provided it is known that the Vi antibody in the sera does not exhibit the peculiar "functional deficiency" described by Felix and Bhatnagar in 1935, the Vi agglutinin titre as well as the O agglutinin titre can be accepted as the final measure of the therapeutic activities of the two antibodies. The routine titration of samples of serum taken in the course of preparation of therapeutic antityphoid sera consists, therefore, in agglutination tests alone.

Dr. D. W. Henderson (Elstree) finds that the Vi or the O antibody will protect mice against infection with a fully virulent Vi+O strain of *Bact. typhosum*; but when a large number of fatal doses are given the Vi antibody is relatively more efficient than the O antibody.

Prophylactic inoculation during a typhoid epidemic.—The desirability of carrying out vaccination in a population exposed to typhoid infection has been questioned on the ground that undesirable reactions may intervene, followed perhaps by frank disease in persons harbouring the causative organisms. Such persons may be incubating the disease—in which case vaccination may, it is said, accelerate the onset of symptoms—or they may be temporary carriers until vaccination converts their state into one of frank infection. Correspondence on this subject appeared in the medical press, two years ago, in the light of advice tendered to authorities concerned with the control of a typhoid outbreak (*Lancet*, 1937, **2**, 1319, 1402, 1454).' In an attempt to find an answer Dr. H. L. Schütze has taken the mouse as the experimental animal and *Salmonella typhi-murium* as the infecting organism. The results of a large series of experiments demonstrate, he holds, not only that vaccination started after infection does not damage the animal's normal resistance, but that in a considerable proportion of cases it actually enhances it.

Plague.—Dr. Schütze, investigating the effect on plague infection of M. & B. 693, Soluseptasine, and a diamino-diphenylsulphone glucoside, observed a considerable curative effect on the part of all three compounds. M. & B. 693 proved most efficacious against plague in both rats and mice; soluseptasine protected rats and not mice; and the sulphone compound protected mice but not rats (*Lancet*, Feb. 4, 1939, p. 266).

SERUM PROTEINS IN HEALTH AND DISEASE

Mr. R. A. Kekwick has continued his work on the behaviour in the ultracentrifuge and electrophoresis apparatus of normal and pathological serum. The electrophoretic constitution of normal human serum has been established and shown to differ fundamentally from the picture obtained with sera from cases of multiple myeloma, kala-azar, and acute rheumatism. The abnormalities found in the protein constitution of these pathological sera were well marked and consistent for a given disease. It is not possible to say how specific they are until a wider pathological field has been investigated.

ENDOCRINOLOGY

Dr. V. Korenchevsky, with the assistance of Miss K. Hall, Mr. R. C. Burbank and Miss M. A. Ross, has further examined the activity of sex hormones in the rat.

Effect on senility.—Testosterone propionate, he finds, can produce in senile rats even supernormal development of the sex organs, but it does not cause any noticeable improvement in their appearance and behaviour. As these organs and sexual function may be well preserved in otherwise senile animals and men, the absence of a "rejuvenating" effect of the sex hormones is held to be not surprising. The over-stimulation of the secondary sex organs of senile rats by testosterone propionate cannot be regarded as a rejuvenating effect, since, without simultaneous improvement of the general condition, this sex stimulation is biologically unnatural "and in human patients is medically undesirable." Moreover, the administration of testosterone propionate depressed the development of the sex glands of the senile rats, thus checking the secretion of the natural sex hormones by the testes. The development of the sex organs may be stimulated or depressed by some of the male hormones according to the dose injected.

Tumours were found in the hypophyses of two of the injected senile rats.

Sex hormones with prolonged activity.—Recently enol and aliphatic esters of sex hormones have been prepared, chiefly by Swiss scientists. The most important feature of these esters is their prolonged activity after the cessation of the injections. With certain of the doses used the maximum effect of testosterone dipropionate and œstradiol dipropionate was maintained for at least 10 days, and that of œstradiol benzoate-butyrate for more than 106 days, after discontinuation of the injections.

"*Precancerous œstrogenic changes.*"—Injections of œstradiol dipropionate are followed, it is stated, by development in the uterus of metaplastic changes in the epithelium, which are the first stage of a precancerous condition. This develops more frequently, or in more severe form, when androsterone, *trans*-dehydroandrosterone and testosterone dipropionate are injected with the œstrogens. On the other hand, progesterone and (when injected in a special ratio to œstradiol) testosterone propionate can prevent the precancerous changes.

ACCESSORY FOOD FACTORS

Progress is recorded in the work of standardising vitamins A, B_1, and E, in the investigation of the B_2 factors, and in the study of pellagra and related disorders of animals.

Vitamin-C requirements of man.—Mr. S. S. Zilva, D.Sc., and Dr. A. E. Kellie have finished an investigation in which the minimum daily dose required to maintain an adult "saturated" in respect to vitamin C was ascertained. Equilibrium of excretion was established on doses of 100 mg., 50 mg. and 30 mg., and the minimum "saturation" dose was found to be in the neighbourhood of the last figure. Previous investigations on animals suggested however that a daily dose of about half the "saturation" dose is sufficient to meet the theoretical requirements of man. The ascorbic-acid content of the blood was determined during "saturation" and "unsaturation" at different intervals after the administration of the vitamin in various doses. The comparison of these figures with those of the urinary excretion suggests that there is no constant renal threshold for ascorbic acid, but that there is a competition for the ascorbic acid of the blood by the absorptive capacity of the tissues and the excreting function of the kidney. Blood levels determined at random do not, therefore, indicate the degree of "saturation."

Vitamin C in vegetables and fruits.—Dr. Zilva, collaborating in an investigation of the ascorbic-acid content of King Edward VII potatoes lifted from the soil at various stages of development, and of the decline in vitamin-C concentration during storage, reports that the content reached a maximum at the third lifting, in early September. On storage at 10° C. the potatoes lifted in October lost the vitamin rapidly at first but later more gradually. The fall in samples lifted before October—i.e., the normal time of lifting—was strikingly greater.

To ascertain the effect of storage on vitamin C in canned apples, samples canned early in 1935 and tested in 1936 were re-examined in 1938. A 50 per cent. loss was recorded; previous intermediate tests had shown this to be progressive.

TYPE CULTURES

The National Collection of Type Cultures (Medical Research Council) has continued to expand. Some 6300 cultures of micro-organisms have been distributed during the year to workers at home and abroad and many new strains have been deposited for maintenance. A new and revised report on the genus salmonella will be presented to the nomenclature committee of the International Association of Microbiologists at the International Congress for Microbiology to be held in New York this autumn. The report is being prepared by the salmonella subcommittee, of which Dr. R. St. John-Brooks, curator of the collection, is secretary.

THE LANCET 100 YEARS AGO

June 29, 1839, *p.* 514.

From a leading article.

A KNOWLEDGE of nature is obtained in two ways,—by observation, and by experiment: *Physicum id est speculatorem, venatoremque naturæ*, says CICERO. We observe, record, and determine the relations of natural phenomena; or we produce effects in order to determine their relations and causes. The experimental sciences, and the sciences of observation are, however, identical; for it is indifferent whether physical phenomena occur spontaneously, or are artificially produced, so far as regards the determination of their laws. But experimental investigation is often more attractive than observation. The observer is a sentinel, a looker-on, or, at the most, a watchman upon the lofty towers of nature; the experimenter, on the contrary, is animated by the pursuit of his game, his blood is heated, his hopes are on the stretch, the forms of truth fly and double, appear and disappear, before the hunter's aching eyes, and the pleasure of the chase is as thrilling as that of the capture. How many have lived and died happy in the search after ideal objects,—for instance, the philosopher's stone and the elixir of life!

GRAINS AND SCRUPLES

Under this heading appear week by week the unfettered thoughts of doctors in various occupations. Each contributor is responsible for the section for a month; his name can be seen later in the half-yearly index

FROM A WOMAN PUBLIC-HEALTH OFFICER

I

THERE is a mocking Gaelic proverb which has ornamented my desk for some years. It runs "He is a good hurler,* is the man on the fence." I love it partly for the salutary warning it holds for the bureaucrat and partly for the picture it evokes. One can feel the wet Irish wind on one's face, and hear the clashing of the hurley sticks, while the excited lad on the fence nearly topples off as he shrieks valueless advice at the straining players. One suspects, too, that the reason the man is on the fence and not in the team is just because he isn't good enough. Some day if he isn't careful fate may play him a nasty trick and bring him down from his perch, thrust a hurley stick into his hand, and bid him get on with the game himself. Even so do I find myself a dispenser and no longer a critic of Grains and Scruples.

* * *

It is a queer business this of turning over the garnered store of nearly forty years to find something worthy of being shared with colleagues known and unknown. A man's most treasured possessions too often seem like junk to the stranger's eye, and his deepest convictions mere infantile prejudices. At this singularly gloomy phase of the world's history when the sky is black with "intimations of mortality" the only sensible advice is that of the evangelical hymn "Count your blessings one by one." Looking back, perhaps the first of these for the young medical student was the contact made at the very outset of one's career with great teachers and great traditions. Perhaps doctors do not always realise that in this respect they are privileged beyond the entrants to other professions. That our best men spend so much time in teaching kindergarten has some regrettable results, but no other system could spread so widely the riches of their minds and personalities.

The arrangement of the curriculum (which I do not intend to discuss) has no doubt improved immensely in recent years, but I doubt if the present-day hierarchy of the profession provides as generous a feast for the observant young as did the professors at my own Scottish university. We still retained the Victorian tradition of highly developed individuality. The pride and joy of the school was a famous authority on forensic medicine equally beloved for the raciness of his lectures and for his discrimination as an examiner. He had an infallible method, worthy of wider imitation, for reassuring a nervous student. On the examination table stood the usual row of evil-smelling little bottles containing material to be "spotted." As the tongue-tied one hesitated the kindly old gentleman, hero of a hundred *causes celèbres*, absentmindedly rotated the bottle so that the label came to the front.... It was said that after a myopic youth had nearly defeated him he always kept a bottle of copper sulphate crystals in reserve for desperate cases. Only once did he fall below his own high standard. Asked to explain his eccentric marking of a brilliant paper presented by a woman student, daughter of a colleague, he is said to have retorted fiercely, "Well he ploughed my son and by gad, I'll plough his daughter"—but quickly repented. Thanks to that generous heart, no policeman's form ever darkened the wards of our great infirmary; Sir Henry thought the suggestion of punishment an outrage on the sick and bullied the authorities into compliance, cheerily regardless of not infrequent escapes.

The women students at least were ready enough to welcome the police as escorts of outpatients. In the cramped little casualty room which was all the territory allotted to us, they subdued our patients' lurid language, taught us how to handle a razor, and told us thrilling stories of the underworld while we stitched cut heads. In those days of cheap whisky one expected most casualties to be drunk, and I can recall a New Year's Day when of 82 accident cases only the first 20 were even approximately sober. The police, who knew the sordid background of their lives, gave us our first lessons in tolerance.

* * *

To return to the more orthodox instructors, many of the great folk round us remained merely names, for the women were kept under as near an approach to the purdah system as a mixed school permits. We were forbidden university lectures, and for clinical teaching were restricted to the wards of the junior surgeon and physician on the staff who had each to put in a purgatorial five years teaching the interloping sex. But we could afford to chuckle at the way things turned out. A system that gave us Professor Caird in surgery and Sir Robert Philip in medicine left no resentment. Caird was a man whose personality should surely be recorded, to inspire other generations as he inspired ours. A magnificent teacher of his subject, he was also supremely successful in conveying lessons that the surgeon can impress on students' minds as no-one else can. Meticulous care in examining and recording the simplest case, and a beautiful courtesy and consideration for patients were part of the routine of his wards. Later, experience in provincial hospitals opened one's eyes to the different standards which existed and I imagine still exist in this respect. It is the sort of thing that in any hospital or institution percolates from above down.

We had luck of another sort in the midwifery lecturer, Dr. Ballantyne. Not that he was much of a lecturer, for only too rarely did he allow his pawky sense of humour or his undoubted vision to overflow into the rather dreary discourses he delivered in the Surgeon's Hall. But one day he abandoned his notes and very shyly confided in his class of some 18 young women his dreams for easing the burden of pregnancy, for making delivery safer by intelligent preparation, for giving the infant a better chance by caring for it throughout gestation. It was a new gospel at the dawn of the century; the class was moved to break into unexpected cheers—and Dr. Ballantyne blushed and retired into his shell. Later he told some of us that he was meeting with little support from many of his obstetrical colleagues who thought that ante-natal care even for private patients was dangerously fussy. The notion that it should be available for *all* women had to wait for a concomitant development of the social health services, in the same way

* Hurley is the Irish version of hockey.

that the aeroplane had to wait for the invention of the internal-combustion engine.

Dr. Ballantyne could get back neatly on some of his critics and I have heard him relate—in private—the following tale. An Eminent Obstetrician who had been engaged for the confinement of a Great Lady, received the call to her bedside towards the conclusion of a very festive dinner. Some inward voice told him it might be wiser to send his assistant but he reflected that the latter was a pushing young fellow and anyway the smell of chloroform *à la reine* covers a multitude of other odours. Everything went swimmingly. It was one of those ideal cases where nature—i.e., the mother and maternity nurse—does all the work. True, the baby was on the small side, but it was of the right sex and the mother seemed more than satisfied. The eminent obstetrician felt fully justified in hastening off to a bed that every moment appeared more desirable, but had only reached the foot of the front doorsteps when he heard his name called. He looked up and saw the nurse grimly regarding him from the doorway, "Well, nurse, have you forgotten anything?" he asked impatiently. "No, Sir, but I thocht mebbe you had . . . the twin."

* * *

Not even a desire to compensate for the news on the wireless could however persuade me that if the hands of the clock could be turned back all would be well. Entrants to the nursing profession may be scarce now, but I should hate to see them plentiful—and bullied and overworked and underfed as they were thirty years ago. Again, over-specialisation may be the curse of the profession, but from the patients' point of view its absence is still more to be deplored. In all that great Scottish infirmary there was no anæsthetist; all anæsthetics were given by students, taught only by their seniors and equipped with a folded towel, a gag and tongue forceps, two safety-pins and a bottle (unmeasured) of chloroform. If a surgeon found (as Mr. Caird once did) during the vacation that his list included an excision of thyroid, a carcinoma of the breast, and an excision of the kidney and the only student on duty was a girl of 19 in her second year, they both went ahead without comment. The results were astonishingly good, but I always felt that the guardian angels of all concerned were being tried rather high.

The chief difference on the debit side, however, was the complete lack of social services, of aftercare to consolidate the good work done in the wards, and of the *preventive* outlook generally. You will still hear modern advances spoken of as though they were an unprovoked attack on an ideal system of private practice. One remembers how much of the illness one saw was due to deficient nourishment and to an inconceivable filth of hair and person. The only preventive measure that occurred to anyone was to blame the unfortunate mothers or to proffer them lordly advice on a matter on which none of us, male or female, had the slightest experience—i.e., running a working-class home on a working-man's income. I count it not least of our blessings today that the working-woman is no longer a bundle of squalid rags surrounded by rachitic and verminous children.

* * *

A batch of papers from a college for "nursery-nurses" has just come in for correction. Written in clear round hand this statement catches my eye "The skin contains salacious glands . . . and censory nerves." How wise are the dispensations of providence.

PUBLIC HEALTH

School Medicine in Manchester

IN an introduction to his valedictory report to the Manchester education committee Dr. Henry Herd discusses briefly the two chief contentions with which his name is associated—the relations of the school medical officer with the public-health service and education department, and the place of routine inspections in the medical supervision of school-children. Manchester is one of the few localities where the medical officer of health is not the school medical officer, the latter being appointed by the education committee and having no official connexion with the health office. But in most large local units the executive school medical officer, though nominally an assistant, is largely independent of the medical officer of health who contents himself with coördination of the school service with the rest of his department. So in practice it makes little difference whether or not the school medical officer is independent of the medical officer of health, provided that there is complete cohesion between the two officers; and in recent years this has been generally achieved. Unless there is close coöperation between school medicine and child welfare reduplication of effort occurs, the children lose continuity of supervision and many matters which should be remedied in infancy are deferred until school age. Moreover, the health of children attending school is much influenced by the variations of infectious diseases; the school officer must be in touch with the officer whose chief function is epidemiology. On the other hand, school medicine is intimately connected with education. As Dr. Herd says, "the school medical service can never be a purely medical service, but must be very closely identified with the general educational service." The bond between school medicine and general education grows closer, as the fitting of abnormal children to their educational environment is becoming the chief work of the school medical officer.

Dr. Herd has for several years urged reform of the system of routine medical inspections. At the congress of the Royal Sanitary Institute, held in Bournemouth in 1935, he was one of the leaders of the reform party which sought to replace routine inspections at fixed times by more general inspections of all children at shorter intervals and continuous supervision of those who were defective, or whose health or normality was doubtful. The case of the reformers is very strong, although for their system to be successful more labour and greater skill are required than can be commanded everywhere. The Board of Education makes routine inspections the cardinal point of school medicine; those who think with Dr. Herd look upon them merely as adjuncts to continuous supervision. In districts where the school department is properly staffed all that Dr. Herd advocates could be obtained without abolishing any of the routine inspections—to a large extent he has himself achieved it.

The records of the school medical department of Manchester do not differ materially from those of other cities. There has been the same steady improvement in the health and physique of the children, similar increased attention to matters formerly considered to be of minor importance, and an increase in the

quality and expedition of treatment for those children who need it. In Manchester a definite improvement is shown in children as they grow older: of the entrants 22·8 per cent. required treatment, of the twelve-year old group only 14·7 per cent. Most of the conditions calling for treatment were either trivial blemishes, physiological deviations, or minor ailments to which little attention was paid before the development of school medicine. The most important purely medical work of the school department is in connexion with abnormal conditions of the upper respiratory tract. These include tonsils, adenoids, enlarged glands, nasal catarrhs, and otorrhœa. There was a time when all manner of evils were attributed to adenoids and the T. & A. operation was regarded as the remedy. It is now agreed that upper respiratory catarrh is a highly complex matter, involving many factors and calling for many forms of treatment, amongst which removal of adenoids or tonsils or both still occupies an important place. Otorrhœa and nasal catarrh, though they have diminished greatly in frequency, are still amongst the chief worries of the school medical officer. To Dr. Herd and his generation, acting with throat specialists attached to the school department, we owe most of our present knowledge of upper respiratory catarrh at school age. In this report much space is given to throat and nose defects, including an account by Mr. Brian Robinson of the results of diastolisation, which should be read by all who are not familiar with this form of treatment.

During Dr. Herd's tenure of office great advances have been made in child guidance, and, in coöperation with the physiological department of Manchester University, work has been done in genetics and physiological variations which are gradually changing the outlook of school medicine. When he started the chief work of the school doctor was to detect and obtain treatment for children suffering from diseases and defects which should have been detected and treated before; his main work has shifted to fitting to their environment individual children deviating from normal.

PARLIAMENTARY INTELLIGENCE

ON THE FLOOR OF THE HOUSE

By MEDICUS, M.P.

THIS week has been remarkable for two defeats of the Chancellor of the Exchequer. The first defeat was one by negotiation, that in which the Chancellor withdrew the duty on films. The explanation then was that it had not been possible, because of the need for secrecy in all Budget arrangements, to consult the trade and that an error of calculation had been made. Perhaps. But on this the House remained slightly sceptical. Whatever the reason however the withdrawal of the duty, a defeat by negotiation, happened. The second defeat was a defeat by argument and organisation inside the House of Commons. The Chancellor had proposed to repeal the duties on patent medicines and the excise licence but had not proposed to control the sale of patent medicines or appliances or any of the preparations which come within the description of proprietary medicines in any alternative way. The duty was to be repealed and the field left open without any attempt at control. This proposal attracted a great deal of attention as soon as it was known after the Chancellor had made his Budget speech. The Medical Parliamentary Committee considered the matter and its members, who belong to all parties in the House, consulted with their friends as to what was likely to be the outcome of this proposal.

It was agreed of course that the duties were archaic and in need of revision. A select committee of Members of the House of Commons had reported in that sense as lately as 1937. But this committee, which was unanimous, proposed an alternative method of taxation and a further control not only of medicines but such apparatus as deaf-aids and such substances as quasi-medicinal beverages and quasi-nutritious foods. To have the whole of these very carefully considered recommendations brushed on one side was more than the members of the select committee could stomach.

In a very short time it became clear that a large body of opinion in the House of Commons was opposed to the repeal of the patent medicine duties unless they were replaced by some alternative method of control. The existing amount of control by taxation and licence is not great but to repeal the duties would have thrown the patent medicine trade wide open. The pharmaceutical chemists had also considered the question and they added their influence to the persuasions of the already informed members of the House of Commons, and, at a later stage, circularised all members and pointed out, among other things, that in case of repeal of the duties "unless some further change in the law is made any person or persons can, from September next, make and supply medicines to the public through any vendor or automatic machine, without disclosing the composition of the medicine sold. This will most likely result in a great increase of so-called cures of unknown content for self-medication, which would constitute a grave public danger."

The pharmaceutical organisations and individual chemists were not, however, the origin of the opposition to this repeal. They came indeed fairly late into the field. It was organisation inside the House of Commons by the Medical Parliamentary Committee and the members of the select committee that started the ball rolling. By Thursday, June 22, when the Finance Bill came up for discussion in committee of the House, opposition to the duties had so hardened that as many as 200 supporters of the Government, led by Sir Francis Fremantle, were asking for the postponement of the repeal for some years—which was of course equivalent to rejection. Another amendment, put down by Mr. Lewis Silkin and Dr. Haden Guest of the Labour Party and Mr. Gwilym Lloyd George, Mr. Graham White and Sir Percy Harris for the Liberal Party, was supported by over 50 names, and there was only a small minority of members in either opposition party who were in favour of repeal. The remarkable situation was presented of a large proportion of members of all parties being against the abolition of a tax—quite contrary to usual parliamentary procedure. But up to the actual time of the debate on Thursday evening—which was, unfortunately for purposes of press publicity, at a very late hour—the Chancellor had given no indication of his attitude.

* * *

The attack was launched by Mr. Graham White for the Liberal Party, who recalled that on the second reading of the Finance Bill the opinion of the House appeared to be against repeal and said that the more

he considered the matter "the more inadequate" seemed the reasons advanced for the abolition of the duties. Mr. Graham White had hoped we were moving towards the adoption of a nation-wide medical service but the proposed repeal was an attack on the national health service; and he recalled how the Ministry of Health had deplored the use of advertisements and quack remedies in connexion with cancer. The Chancellor of the Exchequer would, however, open the way to the sale of any nostrums or quack remedies. Sir Arnold Wilson, who was a member of the select committee which reported in 1937, urged retention of the duties for a further period of at least one year in order to replace them by "something better and more effective." There was no reason for precipitant action as the duties had "been going for 100-odd years and can very well go on for another year"; meanwhile the Chancellor would be "in a position to reconsider the whole thing in all its bearings, which are much wider than those merely of the revenue." Sir Arnold Wilson saw no objection to taxing proprietary medicaments and preparations, "whether medicinal or quasi-nutritive, whether aids to beauty or to health, to sleep or to relieve pain." If the duties were repealed, he said, we should be "the only country in Europe and almost the only country in the world except the United States . . . where patent medicines and proprietary medicines are not taxed." It appeared that alternative schemes had not been discussed with representative interests and some of the largest druggists in the country had said they were not consulted. The National Pharmaceutical Union and the Pharmaceutical Society of Great Britain were not consulted. The point in Sir Arnold Wilson's admirable speech which attracted most attention was that in which he quoted the Chancellor as saying: "Not only are the present duties unworkable—they are being worked unlawfully and our action has been challenged," and he recalled that the firm which had thrown down this challenge was F. W. Woolworth & Co., whose managing director appeared before the select committee to give evidence. "The managing director said he wanted to sell more drugs, and he could sell far greater quantities in 2*d*. or 3*d*. packets than in 6*d*. packets and the stamp duty prevented him selling his smaller quantities." If it was necessary to meet this challenge of an action for damages Sir Arnold said "many of us" would have preferred to see the Government lose the action. The situation could have been dealt with by retrospective legislation, because, although this course is disliked, in principle if anyone in the country "puts a pistol to the Chancellor's head, we would willingly come to his support." Sir Arnold considered that if the taxation of cosmetics was added to that of medicines the duty would bring in from 3 to 5 millions, an important amount of revenue, and taxation would facilitate control.

Dr. Haden Guest dealt with the matter entirely from the health point of view and described the proposed repeal as "an attack upon the health of the people." It would be a grave injury to health although of tremendous advantage to certain large interests. The proposal to repeal was received "with a whoop of joy" by certain circles in the city. There had been some big financial flotations and "inflations of a really disgraceful character in the patent medicine racket" in recent years. There is a great amount of money in the trade; the select committee calculated it at £20,000,000 a year on a moderate estimate and it was a trade built up, in the words of the select committee, "by making the people, largely the poor and less well educated, spend more money than they can afford on remedies of little or no efficacy with an accompanying indirect danger to health as a result of their not seeking medical and surgical treatment in time." It was a trade based "on an appeal to fear." Dr. Guest proposed that if the Government persisted in the repeal the Government front bench should give "an unequivocal undertaking and understanding that they will bring forward legislation to control the whole of the patent-medicine and patent-instrument industry."

The debate was one very largely in the hands of the medical M.P.s, the two next speakers both being doctors. Sir Henry Morris-Jones urged the Chancellor to give way to the arguments which "represent a very strong feeling in the country" and he was mystified as to why, at this time, the Exchequer should "throw away a matter of £1,000,000 a year" in taxation.

Dr. Edith Summerskill agreed with Sir Henry across the floor of the House and said that if the Chancellor repealed the duties "he will be aiding and abetting a gigantic swindle throughout the country," and she gave examples of the constituents of certain patent or proprietary medicines. She asked the House to imagine what would happen "when the whole market is flooded with these people, who are just waiting to deceive." No-one spoke for the Chancellor until Mr. A. V. Alexander of the coöperative movement, and he was lukewarm as he said the coöperative societies "had always been against the wide advertisement of worthless remedies." The House however, including the Labour Party, was so impatient of Mr. Alexander's tepid support that he had to reply to an interruption by saying "I hope the Committee are prepared to listen," and there was a good deal of interruption later.

Sir John Simon to conclude the debate made a half-hour speech of exposition of the reasons which had led him to propose the repeal of the duties and referred to "the existing bungle of ancient statutes on this subject" which were "little more than a lot of incomprehensible irrelevancies." The Chancellor was subjected to a number of questions on his speech, by Sir Francis Fremantle, Sir Arnold Wilson, Mr. Latham, a member of the select committee, and others. But the victory of the House, led by medical opinion, over the Chancellor was signified when he said that the sense of the committee evidently was that they would like to get some new treatment of the problem of patent and proprietary medicines combined with the repeal of the duties. "I have no doubt," he said, "that is the feeling of a very large part of the committee. I do not myself feel at all confident that that can be done." The Chancellor then announced that he would be willing to maintain the duties for another year with a view to reconsideration of the whole position.

* * *

The debate was a notable one, but a debate which finishes after half past eleven even although very lively does not get well reported in the daily press. But the debate showed the influence of well-informed opinion outside the front bench circles. The vote was left as a "free" vote by the Labour Party, and the Government whips were quite unable to get their supporters to vote for the Chancellor on this occasion. Danger remains however, for an "industry" that at a moderate estimate is worth £20,000,000 a year is a very big vested interest. It is fortunate therefore that the medical and pharmaceutical professions have shown themselves so much alive to the public-health aspects of these duties and that members of

the House of Commons have shown themselves willing and able to take independent action. The general conclusion, among members of all parties of the House after the debate, was that it was a glorious victory for democratic institutions. As one member put it, "the House just would not have the repeal of these duties."

FROM THE PRESS GALLERY

The Decline in Population

IN the House of Lords on June 21 Viscount SAMUEL called attention to the prospective decline in the population, which was causing widespread concern. In the age of Malthus the great problem was how to check the increase of population; now the situation was entirely changed. While the production of foodstuffs and other commodities had vastly increased, the means had been discovered to control the birth-rate, and the increase in population would soon be replaced by a decrease. It was not enough merely to take the crude birth-rates and death-rates of the population and compare them; the future depended on the age-constitution of the population and on other factors. The chief point, he said, for consideration was the number of live births per thousand women of possible childbearing age, taken as being from 15 to 45. In 1891 this number was 109·8 in England and Wales. At the last census in 1931 it had fallen to 64·3. In the 'nineties one out of every four women between these ages would give birth to a child in any particular year, as against only one in eight in the 1930's. That was a remarkable and unprecedented change not spread over centuries, but taking place in the course of a single generation. There had been, of course, some counterbalancing factors. The death-rate had fallen greatly, though not so greatly as the birth-rate. In 1891 the rate was 19·7 per thousand; now it was about 12·4. In particular the infantile death-rate had fallen with great rapidity. During the present century the strenuous efforts by the state, local authorities, social workers and the medical profession to reduce the death-rate had had a phenomenal success. In 1901, when this movement really began to take effect, the number of infants under twelve months who died was 140,000, or one in seven of all the births of that year. Now the number had been reduced to 35,000, or one in sixteen of the births. That was to say that 100,000 babies who would have died in the previous generation were now saved. Another counterbalancing factor was the fact that instead of people emigrating in thousands to the Dominions, the United States and elsewhere, there was an inward movement on balance of 20,000–30,000 people. But these factors were far from counterbalancing the fall in the birth-rate.

ECONOMIC AND STRATEGICAL RESULTS

Various hypothetical estimates had been made, Lord Samuel continued, of the result of these trends if continued into the future. Dr. Laybourne had concluded that by 1970 the population of England and Wales would be reduced from 41 million to 30 million. Another estimate by Dr. Charles showed that the actual decline would begin in 1941, and that at the end of this century the population would be reduced by half. Of that reduced population nearly half would be over sixty. These calculations might prove wrong, but they demanded immediate attention. Some thought that this country was overpopulated, and that it would be no bad thing if we were reduced even to 20 million. But the truth was not that this island was overpopulated, but that its population was badly distributed. Overcrowding in England was far worse in the 19th century, with a smaller population, than it was today. From the economic point of view a decline in population must mean a great diminution in productive power. Again some held that because there were 1½ million unemployed the country must be overpopulated, and that if our population were reduced by that number, we should get rid of the unemployment. In the 19th century, when the population of England and Wales was 10–15 million, there were periods of terrible unemployment and distress, whereas in the year before the late war, when the population was 36 million, everyone was employed. It was obvious how grave would be the effect on revenue if the number of producers and taxpayers were seriously reduced, and the burden of pensions for an older population, and the heavy charge of debt which was being handed on to posterity, could hardly be borne by a greatly diminished population. There was also the strategic aspect. The man-power of a nation was an essential element in preserving its position in the world. Unless the tide of emigration could be again enabled to flow England would not be rendering the service to the world she was able to do in previous generations.

ITS ÆTIOLOGY AND TREATMENT

The causes of the decline, which was not limited to Great Britain, were due to no physiological change in the human race but to deliberate conscious human action. Children were not born because prospective parents did not wish them to be born, and had found means to prevent conception without forgoing marriage or intercourse. The reason for this state of affairs was largely economic—poverty, or the fear of poverty. Furthermore, parents had to consider the interests of the children they already had from the point of view of nutrition, education and general prospects. There was also the question of housing. Among the non-economic reasons was the health of the mother, which was prominent in the minds of many prospective parents.

There were some, Lord Samuel said, who suggested that the practice of contraception ought to be suppressed by law. The Departmental Committee on Abortion said in its report:

> "We cannot accept the contention put forward in some quarters that the use of contraceptives to avoid pregnancy is fundamentally and in all circumstances wrong, and we doubt whether that view would be shared by more than a minority of persons in this country."

Even if suppression were attempted it was highly improbable that it would succeed. Contraception was not the cause of the decline; it was the means by which it was effected. The better course would be to remove the real cause—the desire for smaller families. From the economic aspect a most effective means of doing this was the institution of family allowances as part of, or supplementary to, the wage system of the country. In France such allowances had been adopted for many years, and now 7 million workers were covered by wage schemes involving allowances. That meant the great majority of the workers of France. No less than £20 million was distributed in France in 1937 in family allowances and the amount this year and last year would probably be far more. There were also limited schemes in Belgium, Germany, New South Wales and New Zealand.

It was necessary to make childbearing as safe, as painless and as inexpensive as possible for every mother in every class of society. The question of extending national health insurance to the child dependents of contributors was also important, as was the campaign for better nutrition. The removal of the marriage bar in certain occupations, and extended income-tax reliefs for wives and children deserved consideration. A definite population policy was needed, and attempts should be made to turn the current of public opinion in favour of marriage and parenthood and not against them. The whole matter, especially the question of family allowances, should be investigated by a Royal Commission.

Lord SNELL did not expect the fall in population to be calamitous. He believed that the real problem of population was qualitative rather than quantitative; that it was darwinian rather than malthusian. The late war robbed the country of something like a million potential fathers. War itself was dysgenic in its effects; it took from the population the most

vital members and left behind those whose vitality was not so great. It was possible that this was only a temporary period, and that a new equilibrium of population would later be established.

A MEDICAL VIEW

Viscount DAWSON OF PENN agreed with Lord Snell that they must consider the quality of the people far more than their forefathers had done. The day had gone by when there were a large number of children born and Nature took off the weaklings. Today the nation was very properly trying to preserve its people, and something had to be done to take the place of Nature's methods. But the graphs authoritatively issued showed that the fall in population was too great even if they did have regard to quality. This country had failed to reproduce itself since 1925. In 1880, the peak year, 100 women during their fertile period produced 150 girl babies. That was no doubt in keeping with the views on population of that particular period. No-one would wish that 100 women should produce 150 future mothers today. Now 100 women produced only 76 girl babies or future mothers. The curve had flattened out during the last two or three years, and Lord Dawson hoped that was a portent of better things. But however much they regarded quality they must have a big enough population to have an adequate turnover if they were going to bring the young people and the fit people to the top. The composition of the population was even more important than its numbers. In 1881 the proportion of people over sixty to those under twenty was as one to six. In 1931 the proportion was as one to three, and next year it would be as one to two. If the present trend went on, by 1960 there would be an equality, one and one, and that meant that there were not enough young lives coming in at the bottom to reinvigorate and replenish the nation. Already there was more accommodation in the schools than there were children to fill it. A change might come, but the curves did not point that way at present.

It was sometimes said that the effect of civilised conditions was to reduce the amount of fecundity of both men and women, but there was no evidence of any mass tendency in that respect. The dominant immediate cause of the diminished size of families was contraception, which was extending in all classes and in all creeds. Contraception had come as the result of social changes; it was not due to a double dose of original sin, but to the evolution of life. It was only a specialised example of man's gradual control of natural forces. One of the things that made contraception inevitable was the reduction in infant-mortality. The safety-valve of a high death-rate was taken away, too many children lived and therefore it was economically impossible to keep them. A way out had to be found somewhere. The woman of today was determined that her maternity should be a matter of choice not chance. She made her maternity a planned part, not the wasteful whole of her life through twenty years, as used to be the case. The chief reason why families were kept down was anxiety in some form or another. Before contraception was an established institution marriages in the early twenties were often impossible. Broadly speaking, he did not see any disadvantage in contraception provided parenthood was not postponed after the age of 25, but there was the risk that people would be apt to extend the childless period too far.

Lord Dawson suggested that the first remedy was further knowledge, which would allay fears about maternity, give instruction and bring home to people a sense of values. A parenthood instruction service should be set up. If they taught people how to rear babies in the child-welfare centres, was it not reasonable to go a step further back and teach them the wisdom of producing them?

The second remedy he suggested was social and economic. Parents who were otherwise willing to bear their quota of children should not be financially penalised. The state should help with some form of allowance which should relate to the children and not to the workers. It should be payable to the mother, if possible, and should relate to welfare and have little or no connexion with wages. If it was paid by tokens they should ensure that the money should go towards nutrition. The tokens should secure milk and such like things for the children. In regard to housing, they must provide for small communities in such a way that the children could have easy access to the air, and creches, nursery-schools, and other necessities should be provided. If provision was made for continuous education after leaving school some of the difficulties they were discussing would be dissolved.

THE NEED FOR MORE DATA

Lord STAMP urged the necessity of a quinquennial census. He argued that if during the past century, with a much more leisurely time-limit of change than existed today, a ten-year census was right, surely something more frequent was necessary now. The fertility inquiry of the census of 1911 should, he said, be reintroduced. That should take precedence of other inquiries, for the information was urgently wanted by the bodies which were considering these problems. At the moment all their calculations had to be based on foreign comparisons. The question of the number of children born of each married woman, the number of children still living, and the duration of marriage were not merely academic questions to satisfy statisticians, mathematicians and population experts. They were the essential basic information, not merely for population problems but also for housing. A gap was left in our recent population statistics which the Government could fill. The occupation of the husband was done now by a schedule that was positively rudimentary and probably dangerous, or at any rate misleading. This ought to be made similar to the census of occupations. If they were to devise any rational policy they must know what the net reproduction-rate was for those in certain occupations or belonging to certain classes.

Lord TEMPLEMORE, replying for the Government, said that this was eminently a subject where they must have reliable data, and complete data were not yet available. The most comprehensive material they possessed was at the disposal only of the Registrar-General, and his experience suggested that some of the published forecasts expected an earlier decline in population than the facts justified. Some of the estimates made had already been falsified or discarded, and during the last six years the realised experience had pointed to a postponement of the date when a decline was possible. For the first time since 1873, the beginning of the decline, the birth-rate began to rise in 1934, and that tendency had continued unbroken for five years in succession. Whereas the percentage of increase of population fell till in 1933–34 it was 0·31 per cent., in 1934–35 it had risen to 0·43 per cent.; in 1935–36 it was 0·45 per cent., and in 1936–37 0·44 per cent. In 1937–38 there was a little decline to 0·42 per cent., but these figures emphasised the need for caution in forecasting future figures. The marked check in the decline of the birth-rate during the past five years might be associated with the relative economic recovery of the country. Without suggesting that a decline in population was not a possibility after the next fifteen or twenty years, he thought that the matter was far more open than was generally believed. A number of countries had adopted family-allowance systems, but in general it was not possible to detect any significant association between the allowances and the birth-rate. The only country with a record of a material increase in its birth-rate ensuing apparently from statutory political measures was Germany, where the rate rose from 14·7 per thousand in 1933 to 18 per thousand in 1934. For this change the introduction of a system of non-interest bearing marriage loans, 25 per cent. of which was cancelled on the birth of each child, was held to have been partly responsible. There was a considerable difference of opinion about the desirability

of adopting proposals of this nature. The more sensational and pessimistic forecasts of population had been based on the assumption that the birth-rate would continue to decline below the 1933 minimum of 14·7 per thousand; whereas if the present level was maintained, even without further improvement, it was unlikely that the population would fall below the current total of 46 million for two or three decades. They needed far more data before they could reach a basis for Government policy or action. The Government had already taken steps to collect such data. From the Population (Statistics) Act, 1938, which came into operation on July 1 last year, information would be obtained which would throw a valuable light on the varying incidence of fertility in different sections of the population, and a body of data would be built up from which details of the changes taking place from time to time would be immediately detected. The collection of these data would, of course, take time. Even if this did not directly reveal the basic causes of these changes, it would serve as an indispensable background of fact, both for the testing of variations in regard to the previous basic factors, and also for estimating and measuring the results of any concerted attempts to vary their natural course. When the data became available they would be able to see whether the position was such as to demand action, and, if so, what action would be most likely to prove effective.

Medicine Stamp Duties Retained

In the House of Commons on June 22 the clause in the Finance Bill repealing the medicine stamp duties was considered in Committee. Mr. GRAHAM WHITE said that it was not the duty of the Government to abandon revenue simply because they had reason to apprehend difficulties in administration. If they threw over these duties and allowed the sale of remedies to go on without let or hindrance as to place, quantity or description that could only be an attack on the national health service of the country.

Sir ARNOLD WILSON did not think there had been another occasion within living memory when more than 200 members of the House had begged the Chancellor of the Exchequer to continue a tax. There was general agreement that the present duties were archaic and should go, and also that they should be replaced by something better. If this clause were omitted from the bill the Government would be given the opportunity during the next twelve months to reconsider the whole subject. The repeal of these duties would, unless others were substituted, facilitate the expansion of a trade which, to put it mildly, urgently needed control and restriction. The chief medical officer of the Ministry of Health in his report for 1934 almost invited the taxation of medicines, even of the sort prescribed by doctors. He said:

> A considerable proportion of the total outlay on drugs prescribed by the medical profession, averaging 3*s.* per head, could be limited without detriment, indeed with advantage and to the proper treatment of the people.

Oliver Wendel Holmes went further when he told Harvard medical school:

> If the whole materia medica could be sunk to the bottom of the sea, it would be all the better for mankind, and all the worse for the sea.

Sir Arnold Wilson's nurse put it still more succinctly:

> Remember, child, that doctors think
> More men have died from drugs than drink.

No attempt, he said, had been made to devise an alternative scheme. Was it to go on record that no scheme could be evolved by the Commissioners of Customs and Excise for a reasonable tax on medical preparations? He was assured that there had been no consultations, officially or unofficially, with representative interests. He agreed that pharmaceutical chemists had had a certain protection hitherto, but the 200 members of the House who were opposing repeal held that those chemists should have that protection. They ought to be protected from competition by grocers, cheap-jack stores, and hawkers. The repeal of the tax would discourage the publication of formulæ, a matter of real importance. Most members had lost all hope that the Ministry of Health would promote a bill dealing with proprietary medicines. At least ten attempts had been made by private members to get such a bill through Parliament, but they had all failed. Now, in the 5*s.* stamp booklets to be bought at post-offices, drugs were advertised which had been specifically banned by name as fraudulent by the whole press of Fleet Street. The Minister of Health ought to bring in a bill to prevent his colleague from advertising medicaments which were notoriously dangerous.

Dr. HADEN GUEST said that the repeal of this tax amounted to an attack on the health of the people of this country. It would, of course, be of tremendous advantage to certain large interests. The work of the patent-medicine vendor was based on the exploitation of fear, and was buttressed by the prostitution of medical terminology in the service of boosting quack remedies. If this proposal passed, the Chancellor of the Exchequer would be immortalised in the future as the "stop me and buy one" Chancellor of the patent medicine industry.

Sir HENRY MORRIS-JONES said that not only the retail chemists, but all the drug trade, all the medical profession, and a large body of public opinion in the country were completely mystified as to why at a time when the state was in greater need of revenue than it had been in living memory, they should throw away a tax bringing in a million pounds a year, while at the same time jeopardising the public health of the country.

Dr. EDITH SUMMERSKILL said that if this clause was allowed to stand the Chancellor would be aiding and abetting a gigantic swindle throughout the country. An opportunity would be given to every bogus patent-medicine vendor to flood the market with any preparation he liked without obligation to put the formula on the box. A few months ago there were certain preparations on the market containing iodine which were being used by young girls for slimming. It was exceedingly dangerous for young girls to use iodine preparations. There were two or three fatal accidents as a result of overdoses, and these preparations were withdrawn. Now it was proposed to open the market again to those who put on to it these harmful drugs.

Mr. ALEXANDER urged that where the formula of secret remedies was not disclosed to an independent and qualified body, that particular commodity should be banned. If they really wanted to control patent medicines in the interests of the health of the people, such commodities, whether dispensed by a pharmacist or not, should be banned altogether.

Sir JOHN SIMON, Chancellor of the Exchequer, said that it was not very likely at this time of day that he wished to lose revenue. These medicine stamp duties were one of the curiosities of the statute book They had been described by a learned judge as "a mass of confused and obsolete verbiage." They were 130 years old. They were enacted at a time when ideas about medicines and cures were very different from today, and the attempt to retain them involved all sorts of ridiculous distinctions. For example, the law provided that duty was to be paid if the remedy referred to an organ of the body, but there was to be no duty paid if the same remedy referred only to the organ of the body and did not mention the ailment. If one offered "kidney pills" there was no duty, but if one called them "back-ache kidney pills" a tax had to be paid. It was true that the administration by the authorities of this tax was challenged, and it was a very serious thing for the Chancellor of the Exchequer to allow a challenge to go against a tax which his officers were collecting; all the more so when the advice he was given was that his position was exceedingly doubtful. The truth was that it was impossible to apply the acts as they should be

applied. He could well understand that there were questions of public health and public control involved here; but he could not agree that medicines were a good subject out of which to raise taxation. The select committee in their report recommended that a duty should be imposed on a very wide range of medicines and remedies, practically all medicines and remedies except those made up from the prescription of a doctor. If that was the view of the committee as a whole it certainly did not agree with his view. He had done his best to see if he could find a tolerable modification, but he had failed. The select committee took the opinions of a large number of people, including witnesses speaking for the British Medical Association, who strongly took the view that the existing taxes were not justified, and asserted that if one wanted to try and discourage quack remedies the right way to do it was not by taxation. But having taken evidence the select committee proposed a new scheme of duties. Under their proposals there would have been no preference to chemists at all. A whole range of things would have been brought under the duty, in fact anything except a doctor's prescription. Was it really the general view of the committee that he should have adopted that alternative? This duty did not protect the public health at all. (An hon. member: "Yes it does.") He was only expressing his humble views.

Dr. GUEST: Against all the medical and pharmaceutical profession.

Sir JOHN SIMON: I do not think I can be accused of that, since I am relying on the evidence given by a spokesman of the British Medical Association, Dr. Bowman, who before the committee said he did not consider that the interests of health were to be served by putting taxes on things, but by regulations.

Dr. SUMMERSKILL: ... When a doctor makes a statement of that sort it does not mean that he has circularised the profession and asked their views in any way. He is not speaking for the whole profession by any means; they are his own views.

In conclusion, Sir JOHN SIMON said that evidently the sense of the committee was that they would like, if it was at all possible, to get some new mode of treatment combined with the repeal of the duties. He did not feel at all confident that that could be done, but he was perfectly willing to take the matter up with any other department concerned, and see whether it could. He was willing to maintain the present duties for another year. (Cheers.) In the interval they must see whether it was possible to examine the position both as regarded the possibility of this or any other tax, and also as regarded the aspect of public health.

QUESTION TIME

JUNE 21–28

Medical Examinations of Militiamen

Mr. LAWSON asked the Minister of Labour if he could give the latest figures with regard to the medical examination of militiamen.

Mr. ERNEST BROWN: The number of men medically examined up to June 19 was 49,586. Of these 41,297 or 83·3 per cent. of the total were placed in grade I, and 4553 or 9·2 per cent. in grade II, but of this number more than half were in that grade only on account of defects of vision or feet. The total number of men passed fit for the two grades now being called up for training is, therefore, 45,850 or 92·5 per cent. Of the remainder, 2443 men or 4·9 per cent. of the total were placed in grade III which is the grade appropriate to men who would be fit for certain selected occupations in the forces but are not at present to be called up for the militia. The number unfit for any form of military service and placed in grade IV was only 1293 or 2·6 per cent. of the total. The following table gives corresponding figures for each of the administrative divisions of the Ministry.

MILITARY TRAINING ACT, 1939: ANALYSIS OF RESULTS OF MEDICAL EXAMINATIONS DURING THE PERIOD JUNE 8 TO 19, 1939

Grade.	Numbers medically examined. Division—										Percentages of men medically examined. Division—									
	London	S.E.	S.W.	Mids.	N.E.	N.W.	N.	Scot.	Wales	Totals	London	S.E.	S.W.	Mids.	N.E.	N.W.	N.	Scot.	Wales	Overall per cent.
I	7612	3831	3351	7072	4592	5368	2810	4565	2096	41,297	82·5	84·1	81·5	83·5	85·4	80·3	86·3	84·9	83·3	83·3
II	318	158	167	357	145	343	92	164	132	1,876	3·5	3·5	4·1	4·2	2·7	5·1	2·8	3·1	5·3	3·8
II(a) (vision) ..	457	191	155	321	250	320	117	178	68	2,057	4·9	4·2	3·8	3·8	4·6	4·8	3·6	3·3	2·7	4·1
II(a) (feet) ..	111	68	68	105	69	85	17	75	22	620	1·2	1·5	1·6	1·2	1·3	1·3	0·5	1·4	0·9	1·3
Total of II and II(a)	886	417	390	783	464	748	226	417	222	4,553	9·6	9·2	9·5	9·2	8·6	11·2	6·9	7·8	8·9	9·2
Total of I and II	8498	4248	3741	7855	5056	6116	3036	4982	2318	45,850	92·1	93·3	91·0	92·7	94·0	91·5	93·2	92·7	92·2	92·5
III	508	193	224	420	212	369	132	257	128	2,443	5·5	4·2	5·5	5·0	3·9	5·5	4·1	4·8	5·1	4·9
IV	230	115	145	200	109	200	88	137	69	1,293	2·4	2·5	3·5	2·3	2·1	3·0	2·7	2·5	2·7	2·6
Grand totals ..	9236	4556	4110	8475	5377	6685	3256	5376	2515	49,586	—	—	—	—	—	—	—	—	—	—

The Question of Standard

Mr. LAWSON asked whether the standard for these militiamen had been lowered as compared with the regular soldier.—Mr. BROWN said that the medical examinations of the regular forces had in view the need of particular units, while the examination of militiamen was of a more general character.

Mr. LAWSON: Is the right hon. gentleman aware that the Army report on the conditions of health and examination shows no difference of that kind, and that we have always been led to believe that there was a general standard? Is he aware that his statement has led people in all parts of the country to believe that the standard has been lowered for militiamen and that his answer has given colour to that statement?—Mr. BROWN: That is not so. I am informed that the standards have been changed in some respects in regard to the regular army in recent years. So far from the report showing what the hon. member suggests, if he will refer to the annual reports for 1936 and 1937 he will find the details of these changes.

Mr. SORENSEN: Can the right hon. gentleman inform the House whether the present medical examination is more or less severe than the one carried out during the last war?—Mr. BROWN: It is much more detailed. Hon. members who served last time will know that during the war the examination was conducted by one medical man as a rule. In this case there are four medical men working under a chairman.

Mr. SORENSEN: Is it not true that the length of the examination is only four or five minutes, and in those

circumstances could there really have been a very thorough examination of the militiamen?—Mr. BROWN: I suggest that I arrange for the hon. member to attend at one of the medical boards and see for himself.

Mr. SORENSEN: May I take it that at a very early date after the examinations have been completed we shall have these detailed records in order that we may have a very good insight into the medical condition of an important section of the community, and also in order that we may avoid the impression that prevails in some quarters that under any circumstances the men have got to be inside the armed forces?—Mr. BROWN: That impression is entirely false. I should have thought that every member of the House, and everybody outside, would be proud of the fact that our social legislation within the last thirty years has given us these great results.

Particular Defects

Mr. JOHN MORGAN asked the Minister of Labour if he was aware that X. Y. had been passed as fit for military service even though he wore a glass left eye; and would he state the regulations covering such a decision.—Mr. ERNEST BROWN replied: The instructions to the medical boards provide that persons with one eye only may be placed in grade II and marked "(*a*) vision," provided that that eye is free from disease and reaches a specified degree of visual acuity.

In reply to a further question by Mr. SORENSEN, Mr. ERNEST BROWN said: I regret that it is not practicable at the present stage to analyse the results of the medical examinations so as to furnish statistics of particular physical defects but I will consider what can be done when the examinations are complete. Militiamen with only one eye may, in certain circumstances, be placed in grade II if the other eye is sound. Men with defects of hearing may be placed in grades I–IV according to their condition. The men examined are not tested for colour-blindness. The examination includes a scrutiny of the teeth, and militiamen reporting for training will be fitted with artificial dentures, where this is considered essential, and without charge.

Militiamen and Disability Pensions

Mr. STEPHEN asked the Secretary of State for War if all militiamen who broke down in health during the period of service and were no longer fit for work would be allocated pension in view of the fact that they had been certified as fit men before being called upon to undertake such service.—Sir V. WARRENDER, financial secretary to the War Office, replied: A militiaman will be eligible for a disability award if his disability is attributable to service. It will be appreciated that, although a man may be passed fit on entering the service, he may subsequently acquire a disability, or a latent disability may manifest itself, which has no connexion with his military service.

Mr. STEPHEN asked the Minister to see that the examination was conducted so that latent disabilities would be discovered before the men passed into the army.—Sir V. WARRENDER: I think that is beyond the wit of the medical profession.

Mr. STEPHEN: If it is beyond the wit of medical men, will the Minister see that information is given in every case, when the medical man certifies that the man is fit for service, if he develops disabilities afterwards?—Sir V. WARRENDER: We endeavour to deal with cases in as kindly a fashion as we can, trying to avoid hardship, but it would be impossible to accept liability for all accidents which might happen to a man during his service.

Mr. SILVERMAN asked whether, if the medical examination could not possibly disclose some latent defect, it was possible for medical evidence at a later date, when the defect developed, to be sure that it was not due to military service.—Sir V. WARRENDER said that there had to be some evidence that the man underwent some exposure or hardship during his military service to which his disability could be traced.

Mr. SANDYS: Is it not the fact that six months' training can improve a man's health?

University Students and Military Training

Sir JOHN MELLOR asked the Minister of Labour whether, in view of his consultations with representatives of the universities and schools, he was now able to make a further statement with regard to the antedating of militia training in the case of boys who intended to proceed to the universities after October, 1939.—Mr. ERNEST BROWN replied: Yes, Sir. At a meeting held under the auspices of my department on Monday last between representatives of the committee of vice-chancellors and headmasters, together with representatives of the departments concerned, it was agreed to recommend that boys intending to proceed to the universities were given the double option of postponing or anticipating their liability to undergo military training. I intend to put this agreed conclusion into operation, subject to reviewing the position in twelve months' time in the light of experience, when I propose again to seek the advice and assistance of the representatives of the universities and the schools. It was further agreed at the conference that anticipation of the liability to undergo training in respect of such boys should not be granted to those under the age of 18 years on Jan. 1 of the year in which they wish to take their training. With regard to this recommendation, I cannot do more at present than say that it will be borne in mind when applications for anticipation are considered.

Mr. MANDER: Was this agreement unanimous?—Mr. BROWN: Yes, Sir.

R.A.F. Medical Tests

Mr. GORDON MACDONALD asked the Secretary of State for Air how many applications had been made to join the Royal Air Force during the last 12 months, the number accepted, and how many failed to satisfy the medical tests; and the principal causes of such failure.—Sir KINGSLEY WOOD replied: The total number of applications to join the regular Royal Air Force during the 12 months ended June 17 was 91,447: 41,325 acceptances resulted from these applications, and there were 18,105 rejections on medical grounds. The principal reasons for such rejections were visual defects and physique below the required standard.

Mr. MACDONALD: Can the right hon. gentleman say whether his department take any action in regard to those rejected on such grounds and try to get the disability removed?—Sir KINGSLEY WOOD: I will inquire.

Hospital Staffs and A.R.P. Badges

Mr. HUBERT BEAUMONT asked the Lord Privy Seal why officers and staffs of county hospitals and institutions who had taken the essential courses of training and passed examinations in connexion with air-raid precautions were not being issued with air-raid precautions badges.—Sir JOHN ANDERSON replied: The air-raid precautions badge is intended as a recognition of the obligations undertaken by persons who volunteer for local authorities' and other air raid-precautions services, and persons who take special courses of training in order to enable them to carry out their normal duties under war-time conditions are not, merely by reason of their having undergone such training, eligible for the badge. I understand, however, that the Minister of Health has under consideration the question of providing some other special form of recognition for the staffs of hospitals and institutions in such circumstances as are mentioned in the question.

Civil Defence and Evacuation of Young Children

Mr. DAY asked the Minister of Health what information he had received as to the success or failure of the scheme for registration for the evacuation of children under five years of age; and what steps he proposed to take to ensure the safe evacuation of the younger child population from districts outside the London area.—Mr. ELLIOT replied: I have received returns from a number of evacuation areas which show that the initial response from mothers of children under five has so far, in many cases, been encouraging. The registers are in general still open. In London the returns have been lower than in some other towns, and I would appeal to mothers with young children

to register. The Government evacuation scheme already applies to eleven areas immediately adjacent to the administrative county and to twenty-two provincial areas. As indicated in a reply which I gave on May 18 I am reviewing the possibility of extending the scheme to certain further areas.

Army Rejections on Medical Grounds

Mr. WILLIAM JOSEPH STEWART asked the Secretary of State for War the number of men who enlisted in the Regular Army during 1938 and 1939 and the number of applicants who were rejected on medical grounds.—Sir V. WARRENDER replied: The numbers of recruits finally approved for the Regular Army during the calendar year 1938, and during the period Jan 1 to May 31, 1939, were 38,827 and 20,197 respectively. The numbers of applicants for enlistment into the Regular Army during the periods in question who were rejected at medical examination were 7299 and 3278 respectively.

Mr. GORDON MACDONALD asked for the number of persons offering themselves for enlistment who, on being found below standard, had been sent to one of the recruits physical development depots; and also whether the results had been satisfactory.—Mr. HORE-BELISHA replied: The number sent to the depots is 2775. Of these, 2044 have been posted to units as fit and only 196 failed to reach the standard after training.

Silicosis Scheme

Mr. JAMES GRIFFITHS asked the Home Secretary when the order extending the period of certification under the Various Industries (Silicosis) Schemes would be issued; and if he could state the provisions contained in the order, and whether it would be made retrospective.—Mr. PEAKE, under-secretary, Home Office, replied: The amending scheme was made on June 12 and I understand that copies are now available. The scheme extends the limit in the proviso to paragraph 4 of the principal scheme from three years to five. My right hon. friend was advised that he had no power to make it retrospective. He has, however, suggested, through the Mining Association, that the colliery owners might undertake to deal with claims where the workman has been employed in the mines within the three years preceding the date of the amending scheme, as if the limit in their case were five years and not three. I understand that this suggestion is under consideration.

Young Persons in Factories

Mr. PARKER asked the Home Secretary what representations he had received from manufacturers asking him to suspend the coming into force of section 71 of the 1937 Factory Act on July 1, 1939, and to suspend section 73; and what answer he had given.—Sir SAMUEL HOARE replied: I have no power to suspend either of these sections: but section 71 contains a provision that the coming into force of the section is postponed as respects any particular industry where a public inquiry has been ordered but no final decision has been reached on the question of fixing for that industry a higher figure than 44 as the maximum number of working hours in a week for young persons under 16. A considerable number of applications for more hours than 44 has been received. Many have been refused or withdrawn; in the case of some industries inquiries have been or are to be held; and in the case of some others the question of directing an inquiry is now under consideration. Under section 73 there is power to extend within certain limits the overtime permissible. Regulations for that purpose have been made for various classes of factory, and applications from some other industries for such regulations are still under consideration.

Cheap Milk for Mothers

Mr. TOM SMITH asked the Minister of Agriculture how much of the exchequer subsidy voted under the Milk (Extension and Amendment) Act, 1938, was being used to help maternity and child-welfare authorities to start cheap milk schemes, and the price charged to the local authorities for the milk; how many authorities had inaugurated such schemes and their names; how many expectant and nursing mothers were receiving milk free and for payment, and the price in the latter case; and how much milk was normally given daily in each case and for what period.—Sir R. DORMAN-SMITH replied: While I am hopeful that it will be possible to introduce in the near future a scheme for the supply of milk at reduced prices to English local authorities in connexion with their maternity and child-welfare arrangements, negotiations to that end have not yet been completed. No sums have, therefore, as yet been paid under the Milk (Extension and Amendment) Act, 1938, in respect of milk supplied under such a scheme in England. A scheme has, however, been introduced for the area of the Scottish Milk Marketing Board.

Contagious Abortion in Cattle

Mr. W. ROBERTS asked the Minister of Agriculture whether he proposed that free testing of cattle for contagious abortion should be now included in the provisions of the Attested Herd Scheme.—Sir R. DORMAN-SMITH replied: Under the powers conferred by part IV of the Agriculture Act, 1937, a scheme is being framed whereby owners of attested herds will be assisted, by the provision of free veterinary advice and free blood-testing, to protect such herds as are already free from abortus infection and to eliminate disease from abortus-infected herds. I hope to be in a position to introduce the scheme within the next few months.

Smoke Abatement

Mr. DAVID ADAMS asked the Minister of Health whether he was aware that a pottery factory in Staffordshire had been converted to electric power, whereby smoke had been entirely eliminated; and what steps he was taking to induce other industrialists in the potteries and elsewhere to follow this example in the interests of cleanliness and smoke abatement.—Mr. ELLIOT replied: I am aware that electricity has been used for some time with great success in certain trades in the potteries. My chief alkali inspector in recent annual reports has urged the extension of the practice and has stressed the advantages of electricity and gas where available on economic terms particularly in types of industry that are normally productive of heavy smoke. I have no doubt that smoke prevention authorities and industrial organisations in this and other industrial areas of the country are aware of the possibilities of the cleaner methods, the use of which I greatly welcome.

INFECTIOUS DISEASE

IN ENGLAND AND WALES DURING THE WEEK ENDED JUNE 17, 1939

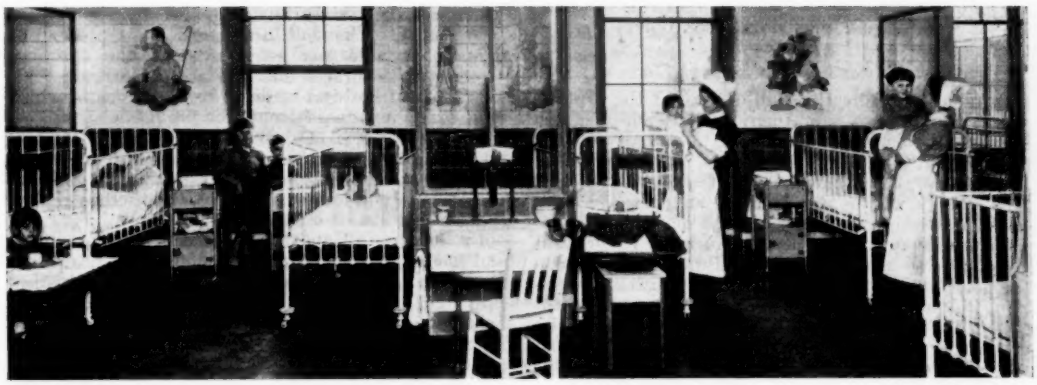
Notifications.—The following cases of infectious disease were notified during the week: Smallpox, 0; scarlet fever, 1549; diphtheria, 755; enteric fever, 21 (28 "expected"); pneumonia (primary or influenzal), 635; puerperal pyrexia, 185; cerebro-spinal fever, 21; acute poliomyelitis, 15; acute polio-encephalitis, 1; encephalitis lethargica, 4; dysentery, 21; ophthalmia neonatorum, 95. No case of cholera, plague or typhus fever was notified during the week.

The number of cases in the Infectious Hospitals of the London County Council on June 23 was 2829, which included: Scarlet fever, 659; diphtheria, 488 (carriers, 24); measles, 8; whooping-cough, 845; puerperal fever, 19 mothers (plus 9 babies); encephalitis lethargica, 304; poliomyelitis, 3 At St. Margaret's Hospital there were 22 babies (plus 12 mothers) with ophthalmia neonatorum.

Deaths.—In 126 great towns, including London, there was no death from smallpox or scarlet fever, 1 (0) from enteric fever, 2 (0) from measles, 14 (3) from whooping-cough, 17 (2) from diphtheria, 30 (9) from diarrhœa and enteritis under two years, and 14 (1) from influenza. The figures in parentheses are those for London itself.

York reported the only death from typhoid. Birmingham had 2 deaths from whooping-cough. Fatal cases of diphtheria were scattered singly over 15 great towns, Liverpool reporting 2. Birmingham had 3 fatal cases of diarrhœa.

The number of stillbirths notified during the week was 218 (corresponding to a rate of 32 per 1000 total births), including 26 in London.

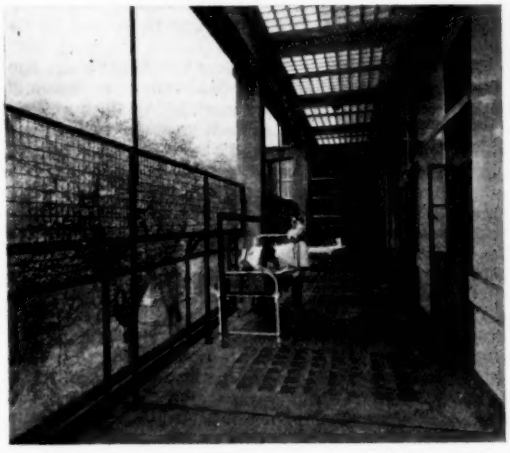


[Bedford Lemere & Co.

Part of Diplock section of ward.

NEW CHILDREN'S WARD AT GUY'S

THE allocation of £21,000 from the estate of the late Caleb Diplock has made possible the construction of a children's ward at Guy's commemorating his name. The new ward is now completed and is one of which any hospital in the world might well be proud, and it is particularly appropriate that Dr. H. C. Cameron should have been invited to remain on the active staff for two years after the normal age of retirement in order to see fittingly housed the department he has built up. The ward occupies the site of the old Bright ward in Hunt's House, and has been reconstructed to provide 47 cots or beds, of which 18 are surgical, 28 medical, and 1 is for the infant of a nursing mother; 10 of the cots are available for paying patients, in order to help meet the increased running expenses of the ward. The ward consists of two main sections (surgical and medical) separated by a main hall. A 10 ft. covered balcony, with a glassed-in playroom for older children at one end, runs the length of the sections facing on to the park, and the windows on this side open to the floor to allow each bed to be wheeled straight out of doors. From the central hall, which is available for demonstrations, sorting linen and so on, open the two sisters' rooms, the kitchen, milk laboratory, pantry, and autoclave room, and the children's operating-theatre and anæsthetic room.



[Bedford Lemere & Co

Balcony of Caleb section of ward.

Both the medical and surgical sections are subdivided into a number of wardlets by glass partitions 6 ft. 9 in. high; the larger wardlets contain 6 cots, and the smaller 4, 3 or 2 cots. An isolation cubicle glassed to the ceiling and having a separate bath and sluice is available for infectious cases. A particularly valuable feature is a small flat for a nursing mother to live in when her baby has to be admitted either for operation or for medical or feeding difficulties. There is a consulting-room for history-taking and the keeping of records.

Each wardlet is provided with a large hand basin, suitably placed and shaped for use as an infant's bath, thus obviating any need for removing infants elsewhere for their toilet. Labour-saving devices include a bottle-washing machine, fixed bedpan sluices and steriliser, an autoclave for infants' feedings, and panel heating in the ceiling with thermostatic control for maintaining the temperature of the ward at 65° F. Perhaps the most obvious attraction of the ward is the light green and primrose tiling of the walls, into which are set coloured nursery-rhyme designs. Each wardlet is fitted with concealed floor lighting and dimming devices on the overhead centre fittings, an advantage in dealing with sleeping children at night.

The ward will be a blessing to the children of "the Borough," and will give lasting satisfaction to the many Guy's men who have long felt its need.

YORKSHIRE TUBERCULOSIS SOCIETY.—This society, which was resuscitated two years ago, under the presidency of Dr. N. Tattersall, has just completed the session with an annual meeting held at Killingbeck Sanatorium by invitation of Dr. W. Santon Gilmour. At the four meetings held during the winter: (1) Dr. Peter Edwards read a paper on methods of obtaining complete collapse of the lung and demonstrated the results of adhesion-cutting. (2) Dr. John T. Ingram proved that, in spite of the chronicity of the lesion, there is great hope for lupus if patient and persistent treatment is carried out. (3) In a paper on the pros and cons of arthrodesis, Dr. H. L. Crockatt professed a conservative attitude although agreeing that cases of non-bony union should be assisted by open operation. (4) Short papers on the diagnosis of abdominal tuberculosis in children (Dr. Margaret Sharp) and cases of transient positive sputum (Dr. S. P. Wilson) provoked lively discussion.

UNITED STATES OF AMERICA

(FROM OUR OWN CORRESPONDENTS)

A MUSEUM OF HEALTH

AT a ceremony in the Hall of Man at the World's Fair on June 17 a new American museum of health was dedicated before an audience of several hundred doctors and public-health officials. Dr. Livingston Farrand, president-emeritus of Cornell University, took charge of the proceedings and introduced a series of distinguished speakers, all of whom emphasised the importance of health education in forwarding the cause of public health. Prof. Abel Wolman, the president of the American Public Health Association, did so by drawing attention to the backwardness of the United States in applying the discoveries of science. He pointed out that although it is an accepted axiom that the individual is the first line of defence against disease, America has the distinction of leading the civilised countries of the world in smallpox, a disease from which the individual can be completely protected. The organisms of tuberculosis and syphilis were discovered many years ago, yet, though progress has been made in controlling tuberculosis, the progress of our campaign against syphilis has been blocked not by scientific ignorance but by social prejudice. The American people are not so healthy as they have a right to be, and in fact public health has never been the first consideration of the state except in times of disaster. Other speakers dwelt on the possibilities of the exhibit surrounding them in the Hall of Man. Dr. John L. Rice estimated that four million out of the seven and a half million persons of New York city would visit the fair, and asked his audience what it would mean to the city if each of them should carry even one idea from this exhibit into their daily life. But the exhibit of the fair is to be only the beginning. A permanent museum housed in the city of New York with its continuous exposure to the population will result in a still greater cumulative effect. Mayor LaGuardia, twitting Dr. Wolman on his pessimism, prophesied that if he were allowed to continue his programme for sanitary housing, nurseries for poor children, and nourishment for the unemployed, tuberculosis would be eliminated in New York city in the next 25 years. But if this end is to be achieved, the responsibility of the government for public health must be recognised. He announced his intention of building a new court-house for the Appellate Division and said that the present fine building at Madison Avenue and Twenty-fifth Street would then be converted into a home for the Museum of Health.

NATIONAL HEALTH BILL

Last month expert medical evidence was offered before a subcommittee of the senate committee which is considering the Wagner National Health Bill. Dr. Arthur W. Booth, who represented the American Medical Association, expressed the opinion that the enactment of this measure "would prove a costly mistake, jeopardising the welfare of the people and seriously compromising the future development of the science and art of medicine in the United States." He said that the projects embodied in the bill had been devised by federal officials and that they do not represent the wishes of the people. The house of delegates in September, 1938, recommended the establishment of a federal department of health with a secretary as its head. The bill provides no such centralisation of authority. The house of delegates also required that expansion of health services should not include provision of medical care, which can be successfully provided by the general practitioner. The bill does not, in Dr. Booth's opinion, provide any safeguards for the existence of the private practitioner. The bill does not limit expansion of hospital facilities to situations in which need exists nor does it limit the provision of medical care to the poor. Dr. Booth felt that the federal bureaus were given too much power over the states, but when Senator LaFollette asked him to indicate the specific powers to which he objected he replied that he had not read the entire bill.

Dr. Richard M. Smith, chairman of the Committee of Physicians for the Improvement of Medical Care, urged the need for coördination of all kinds of medical care under a single administrative authority, aided by a single advisory council. In the organisation of medical care, he said, it is important that public-health services should be under the control of trained full-time salaried experts. The needy should become eligible for medical care without delay or indignity. Provision should be made for the support of education and investigation.

Prof. John P. Peters, secretary of the Committee of Physicians, said that the committee is in general sympathy with the bill. They are interested in strengthening the machinery which can guarantee a high quality of medical care, for this will also protect the public against excessive expenditure. In his opinion the bill is intelligently conceived to meet a demonstrated need. The increased costs of medicine arise not from the rapaciousness of physicians but from the nature of modern medicine. Government aid is made imperative. The bill wisely leaves development and administration of programmes to the several states; it is equally wise in providing that federal authorities shall prescribe standards of qualifications for the receipt of grants in aid.

AUSTRALASIA

(FROM OUR OWN CORRESPONDENT)

NATIONAL HEALTH INSURANCE

THE editor of *Medical Topics* has admirably expressed the situation of national health insurance in Australia: "National insurance has Cheyne-Stokes breathing. Signs of approaching death are evident in the act, but no one in the government has sufficient courage to put the poor thing out of its misery."

For some time it has been evident that the Australian government wants to abandon the National Health and Pensions Insurance Act placed on the statute book last year; but, national insurance being one of the main points upon which the last election was won, such action would require considerable courage—in spite of the almost national feeling against the act—which the government, in an already precarious position, has felt unprepared to show. In March it decided to substitute a medical service plan repealing the pensions provisions and leaving only a system of health insurance and family medical benefit. It was intended to continue the approved society system and the cash health benefits on substantially the same scale as originally provided, but the whole question of medical benefit was to be discussed first with representatives of medical benefit organisations and of the medical profession and later with the consultative council of approved societies.

This substitution of a health service for the original scheme was introduced only at the expense of the

resignation of the attorney-general, Mr. R. G. Menzies. Now, after the sudden death of Mr. J. A. Lyons, Mr. Menzies has been recalled as prime minister to lead a new cabinet. It is doubtful, however, whether this shift of power will make any significant change in the attitude towards insurance. Having so strenuously opposed its abandonment several months ago, Mr. Menzies no doubt feels it incumbent upon him now to make a further attempt to save the scheme. He has promised to ask parliament to set up a committee of members, with whom will be associated representatives of the medical profession and approved societies and the National Insurance Commission, "to see whether a practical scheme, in which all parties will cheerfully and patriotically coöperate, can be evolved."

Appearances, however, are all against the continuance of national insurance. It has been officially announced that it is impossible to bring the health scheme into operation on Sept. 4—the date to which it was last postponed; the National Insurance Commission's activities have been largely suspended; the approved societies have been instructed not to proceed with any further plans; and the royal commission on doctors' remuneration has not been reconstituted since the death of its chairman, has not made a report, and so far has been obviously unable to reach a basis which would ensure the coöperation of the medical profession.

THE NEW ZEALAND POSITION

In New Zealand the question of insurance has taken on a rather different, though equally difficult, complexion. The Social Security Act, 1938, officially began to operate on April 1; but a deadlock persists between the government and the medical profession, and of a possible 750 only 22 practitioners have accepted contracts under the act.

The act entitles every man, woman, and child ordinarily resident in New Zealand to certain benefits, including pensions, unemployment insurance, medical, hospital, and maternity benefits, and the supply of medicine and appliances. Supplementary benefits will be introduced later, such as specialist and consultant, radiological and laboratory, home-nursing and domestic, and optical and dental services. The act ensures adequate services in sparsely populated or isolated areas. Provision has been made for the immediate institution of a health-education campaign, and the scope of medical research is to be extended. The government has given its assurance that the professional standard of medical men and others giving service has been safeguarded; that care has been taken not to disturb the personal relationship between doctor and patient; that all citizens have the right to make a free choice of doctor; and that every doctor will have an opportunity of participating in the service.

However, in spite of these assurances, and since the date on which the act was to come into force, the New Zealand branch of the British Medical Association has unanimously decided that the government's scheme is inadequate and unacceptable, and that its members are unable to coöperate in its administration, being completely opposed to the present scheme, which offers all the people part or limited medical service, as against the association's view that a free complete service should be provided for those unable to pay for it.

Commenting on this attitude, the prime minister has stated that the government, in introducing this legislation, was complying with the wishes of the people—at last year's election the government was returned with an overwhelming majority almost entirely on the question of social security—and that it would therefore make the best arrangements possible to give effect to those wishes. If the profession, under the leadership of the B.M.A., was determined to persist in its policy of opposition, the government would have no option but to alter the whole basis of service and to proceed reluctantly with the establishment of a state medical service to administer the benefits of the Social Security Act. The position is serious for the profession. Ultimately, however, it must be the people who determine what form of medical service they shall receive. In New Zealand it appears they are strongly in favour of a universal insurance scheme, and it behoves the profession to make the best possible arrangements in the circumstances.

LETTERS TO THE EDITOR

PROBLEMS OF DECLINING FERTILITY

SIR,—We should be grateful if we might be allowed to draw the attention of your readers to an inquiry into the causes of infertility which is being promoted by the committee to which we belong. These causes have been much discussed of late in Parliament and elsewhere. It will be recalled that the main object of the Population Statistics Act, which came into effect on July 1, 1938, was to throw further light upon this subject.

But there are strict limits to what we may learn from vital statistics. They can tell us nothing, for instance, about how many marriages are involuntarily sterile or sterile by design, nor of the extent to which abortion and contraception are practised, nor about the numerous motives which restrict parenthood in different regional and occupational groups. These problems can only be clarified by direct inquiry.

A questionnaire has been prepared by our committee. If filled in on a large enough scale it will yield information which is otherwise unobtainable. It has been designed for the use of doctors, midwives, nurses and other competent investigators, and has been drawn up on the same general lines as were followed by Prof. Raymond Pearl in his comprehensive American inquiry. The committee is anxious to obtain records of the attitudes and experiences of as large a sample as possible of married women in this country irrespective of age and parity.

We should therefore be very grateful if those of your readers who are interested in the problems of declining fertility, or in problems allied thereto, would assist the committee by sending for copies of its questionnaire and by filling them in when appropriate occasions present themselves. An honorarium of 1*s.* per filled-in questionnaire is offered. A small manual has been prepared which provides guidance in the use of the questionnaire. Will those of your readers who are interested kindly communicate with the secretary of the Population Investigation Committee, 69, Eccleston Square, London, S.W.1.

We are, Sir, yours faithfully,

EARDLEY HOLLAND,
HENRY BRACKENBURY,
HORDER,
C. P. BLACKER.

June 25.

BLOOD FOR THE SERVICES

SIR,—All those engaged in the present emergency in the organisation of blood-transfusion services in this country would, I think, welcome further information as to the proposed Army blood-transfusion service referred to in your annotation of June 17. For this service it is apparently proposed to draw upon the civilian population for blood for use by the Army. Yet the need of the civil population for blood for purposes of transfusion may, on occasion at any rate, be at least as great as that of the Army.

The need for a nation-wide blood-transfusion service capable of expansion on the outbreak of hostilities is obvious; local effort mainly centred around the voluntary hospitals and without support from any central authority is in many areas doing its best to meet this need. If public funds and the blood of the general population are to be made available for maintaining a blood-transfusion service it seems eminently desirable that it should be for the benefit of all classes of the population, civil and combatant alike.

I am, Sir, yours faithfully,

S. C. DYKE.

Pathological Laboratories, Royal Hospital, Wolverhampton, June 24.

DÉBRIDEMENT AND DÉBRIS

SIR,—My attention has been drawn to the fact that the use of the word *débridement*, in my article last week on the closed treatment of war fractures, is likely to lead to some confusion. The word is the French technical term for incision with opening up of the fascial planes and has no relation to the word *débris*. Where removal of dead or dying tissue was intended I added the words "and excision."

I am, Sir, yours faithfully,

Eton Avenue, N.W.3, June 26. J. TRUETA.

THE PROBLEM OF MEDICAL LITERATURE

SIR,—There is much truth in what Professor McDowall writes. The present state of medical literature is disheartening, but I think it is too pessimistic to assert that there is no prospect of improvement. There is no doubt about the need for greater coördination between medical libraries. Actually librarians do consult and help one another to a considerable extent in an informal manner, and this coöperation is likely to increase. Though various journals may be "scattered all over the libraries of Britain" it is easy to find out where each journal is situated, and at slight expense obtain a photostatic copy of any particular article; it is likely that in the near future microphotography will greatly increase the facilities for such dissemination of knowledge.

It is clearly impossible for every library to take in every medical journal, and if the necessary knowledge is to be made available there appear to be two remedies at our disposal. One is that suggested by Professor McDowall—the publication of a medical abstracting journal, supplemented perhaps by occasional systematic reviews; this would be a great help but would not absolve the student from referring to original articles. The second and in my opinion a complementary step would be the maintenance of at least one large library where all the rarer and more expensive books and journals could be taken; this library ought to work in close coöperation with all other medical libraries, and would need to have a special staff for the work of preparing references and translations, and be equipped with the latest apparatus for photostatic and microphotographic reproduction.

This is the ideal which the library of the Royal Society of Medicine, within the limits imposed upon it, has tried to approach; but it is clear that complete success could not be achieved by any library without endowment.

I am, Sir, yours faithfully,

Harley Street, W.1, June 26. V. ZACHARY COPE.

SIR,—Anyone with practical experience of the matter can hardly do other than agree with Professor McDowall and Mr. Lloyd. No real solution to the problem will be found however until the enormous output of periodical medical literature is reduced by some such drastic measures as those proposed in your recent leading article on micro-films (April 1, p. 765). With regard to a medical abstract journal it might be instructive to know the reasons for the early decease of *Medical Science: Abstracts and Reviews*, which was published by the Medical Research Council from 1919 to 1925.

That medical librarians themselves are becoming alive to the need for closer coöperation is shown by the existence of two recently initiated schemes. The first is an ambitious one organised by the university and research section of the Library Association. A list of all known medical periodicals, of which there are probably about 7000, is being compiled on specially printed cards on which a place is provided for recording the holdings of all scientific libraries in Great Britain and Ireland that possess medical periodicals. This is a large task and may, quite probably, take years to complete. The next step will be to persuade the library committees of the various institutions to cancel redundant subscriptions and, with the money thus saved, to buy other periodicals not at present available.

The second scheme is limited to London and for the present is confined to the four medical libraries of the Royal College of Surgeons, University College, the London School of Hygiene and Tropical Medicine, and the Medical Research Council. A union list of current periodicals has already been compiled and the four librarians have agreed, in cases where there is unnecessary duplication, which subscriptions they will recommend to their committees for cancellation.

The success of all such schemes depends upon the willingness of library committees or other responsible authorities to allow inter-library loans and to sacrifice certain subscriptions. Unless libraries that possess a certain journal are willing to lend it to those that do not, it is obvious that these will not cancel their subscriptions, and unless these other libraries are willing to cancel their subscriptions to redundant journals, there will be no money available for new subscriptions. I should like therefore, through your columns, to appeal to any readers, who may find themselves in a position to exercise authority in such matters, to take the long view and give favourable consideration to any proposals for coöperation on the lines suggested above.

I am, Sir, yours faithfully,

CYRIL C. BARNARD,

Librarian, London School of Hygiene and Tropical Medicine.

Keppel Street, W.C.1, June 26.

LAY PSYCHOTHERAPISTS

SIR,—My committee have instructed me to ask the hospitality of your columns for the purpose of clearing up a serious misunderstanding which seems to exist among medical men about the aims and objects of the Guild of Pastoral Psychology.

The guild desires to equip ministers of religion with sound psychological training so that they may better perform their pastoral duties. It is not attempting to create a class of non-medical persons who would conceive themselves qualified to practise quasi-medical psychotherapy. It envisages as its typical "fellow" a man who holds a cure of souls and who carries out the duties thereof more efficiently by reason of a training in psychology. The guild considers that any minister who wishes to practise professionally as a psychotherapist should conform to the standards to be laid down by the British Medical Association and does not itself at present offer a training to such persons.

Quite clearly, no medical man would wish to claim a monopoly over the whole field of psychology. There is educational psychology, there is commercial psychology, there is industrial psychology—and there is also pastoral psychology. The guild exists to define the limits of pastoral psychology, and the medical members of its committee are there to help it to ensure that pastors do not unwittingly infringe on the province of medical psychology.

I am, Sir, yours faithfully,

BERNARD C. EVANS,
Secretary.

Broadbent Street, W.1, June 23.

MEDICAL NEWS

University of Oxford

On June 21 the honorary degree of doctor of science was conferred on Sir Edward Mellanby, F.R.C.P., F.R.S., secretary to the Medical Research Council.

The John Malcolm Mitchell scholarship, to be competed for by daughters of professional men, will become vacant in October, 1940. Particulars may be found in our advertisement columns.

University of Cambridge

At recent examinations the following candidates were successful :—

THIRD EXAMINATION FOR M.B., B.CHIR.

Part II, Principles and Practice of Physic, Pathology and Pharmacology.—P. S. Adler, G. N. Allen-Williams, R. H. Armin, J. Aspin, D. M. Baker, G. C. Barron, J. R. Bolton, J. F. Buchan, J. H. Burkinshaw, D. L. Caldwell, N. G. Clegg, M. A. X. Cochemé, R. I. G. Coupland, O. J. Curl, J. H. Dean, A. P. Dick, H. J. Dismorr, K. C. Dixon, R. H. Elphinstone, J. F. Erskine, T. Fenwick, A. D. Fisk, W. J. D. Fleming, C. M. Fletcher, R. Fletcher, J. H. P. Gauvain, T. C. N. Gibbens, M. O. J. Gibson, O. D. Gilmore, J. A. Glover, I. R. S. Gordon, G. S. Graveson, A. Hargreaves, G. W. Harris, K. M. Hay, J. M. Holford, W. F. Holman, R. M. Howitt, P. W. Isaac, I. M. Jackson, W. H. Kirkaldy Willis, A. M. Lewis, G. M. Lewis, J. A. Lorimer, F. M. McGown, K. S. MacLean, P. D. MacLellan, J. E. M. Melville, N. E. Monteuuis, E. P. Morley, J. M. Naish, J. C. B. Nesfield, R. O. G. Norman, J. C. R. Nuttall-Smith, A. M. Ogilvie, L. D. Osler, J. N. Pattinson, J. H. Penrose, C. P. Petch, A. Ponder, B. W. Powell, L. M. Reid, W. H. S. St. John-Brooks, P. D. Samman, M. Savory, M. J. Scott, P. D. Scott, J. R. Squire, A. Standeven, A. J. S. B. Tawse, P. S. Thorne, J. S. H. Wade, H. R. E. Wallis, W. H. C. Watson, G. C. Wells, H. W. Whittingham, R. Wilson, and P. N. Witney.

University of St. Andrews

At recent examinations the following candidates were successful :—

FOURTH EXAMINATION FOR M.B., CH.B.

R. M. Bell, J. M. Berry, John Black, K. G. Broadbent, J. S. Brunton, John Cameron, A. J. M. Cathro (with commendation), Elizabeth P. Dodds, J. M. Duncan, A. C. Fraser, Elizabeth N. Harrison, M. C. Hodgson, W. F. E. Immelman, R. S. Kennedy, R. T. Kiddie, Peter Kinnear (with commendation), Douglas Latto, H. L. Lillie, A. R. T. Lundie, Elizabeth T. McDougall, W. T. McGinness (with commendation), Winifred I. McNicol (with commendation), E. G. McPherson, D. J. Macrae, D. S. Milne, Charles Milne, Freda C. J. Nicoll, R. A. Philp, D. V. Porter, G. H. Rea, G. W. Taylor, B. S. Tulloch (with distinction), Kathleen S. Turner, W. A. Whyment, J. S. Young, and John Young.

EXAMINATION FOR B.D.S.

I. M. B. Allan, E. A. Haxton, R. S. Henderson, J. L. Hutton, and R. P. McGlynn.

Botleys Park Colony for Mental Defectives

The new buildings, which are situated in 300 acres of parkland and have accommodation for 1200 patients of either sex, with provision for an additional 300, were declared open last Saturday by Lady Henriques, wife of Sir Philip Henriques, chairman of the Surrey county council. The hospital, built mainly of fireproof materials, cost £530,000, and consists of 21 residence houses for patients, together with a recreation hall with seats for 750, administration and stores buildings, workshop, kitchen, laundry, and school premises. The eighteenth-century manor is being used as a nurses' home.

Prizes at Glasgow

The senate of the University of Glasgow announces that the Struthers gold medal and prize has been awarded to George M. Wyburn, D.Sc., M.B., F.R.F.P.S.G., F.R.S.E., for an important series of embryological studies embodied in papers published in the *Journal of Anatomy* in January, 1937, April, 1938, and January, 1939. The Harry Stewart Hutchison prize has been awarded to James Holmes Hutchison for his dissertation entitled the iron-deficiency anæmia of childhood.

Short Service Appointments in the Navy

The Admiralty announces that the following have received appointment as surgeon lieutenant, R.N., for short service: P. W. Edmondson, M.R.C.S.; E. A. Penn, M.R.C.S.; G. N. Reed, M.B.; J. K. Salmon, M.R.C.S.; and F. B. B. Weston, M.R.C.S.

Extension of Harrogate Baths

Harrogate's new £100,000 spa extension scheme will be opened by the Lord Mayor of London on Monday, July 10. The new scheme provides for an entirely new building, in which exclusively Harrogate mineral water treatments will be administered. The equipment of the building and the treatment apparatus are said to be the last word in spa technique. The capacity of the new building will be a thousand treatments a day. In addition a new lounge hall has been constructed for the recreation of patients undergoing the cure. Between the new building and the lounge hall is a fountain court surrounded by a covered colonnade, heated, and enclosed in glass shutters in winter, where patients may take gentle walking exercise while drinking the spa waters, and between the periods of treatment.

A Postgraduate Class in Dublin

Our Irish correspondent writes: A postgraduate class on, for Ireland at least, novel lines is just concluding a fortnight's work in Dublin. It was novel in that it was organised as a coöperative undertaking by the entire ten general clinical hospitals of Dublin, each hospital acting in turn as host for one day. It differed also from previous postgraduate courses in Dublin in that the tuition was entirely clinical, the medical schools as distinct from the hospitals taking no part in the course. The experiment has proved a success, as far more graduates entered for the course than had been expected—over 70 in all. This degree of popularity was in fact embarrassing as the numbers were too large to render clinical demonstration easy. It became clear that if the class is to be repeated in future years it must be divided into manageable groups. The members of the class and their teachers dined together in the Royal College of Surgeons last Saturday evening under the chairmanship of Mr. William Doolin, president of the College. There were no formal speeches, but the members of the class, on the invitation of the chairman, offered criticisms and suggestions on its future management. An interesting and instructive discussion followed which should help the development of postgraduate teaching in Dublin.

Guy's Hospital

Applications are invited for the Astley Cooper studentship which is tenable at the hospital Particulars will be found in our advertisement columns.

Mental Hospitals Association

The twenty-first annual meeting will be opened by the Lord Mayor of London in the council chamber of the Guildhall at 11 A.M. on Thursday, July 6. A discussion on the Matrimonial Causes Act, 1937, in relation to mental hospital practice will be opened by Dr. T. C. Graves, chief medical officer to the Birmingham mental hospitals committee.

Appointments for Patients at St. Thomas's

St. Thomas's Hospital has introduced a system by which outpatients are seen by appointment. So far only old cases have been catered for but the results have been so encouraging that the system is likely to be extended to new cases as well. The report of the almoners' department foresees the time when "the mere idea that patients, except in an emergency, should come up to a hospital without an appointment will be regarded as fantastic."

Royal Medico-Psychological Association

The annual meeting of this association will be held at Brighton, on July 12, 13, and 14, when the new president, Dr. Helen Boyle, will give an address entitled Watchman What of the Night? and the principal subjects for discussion will be early treatment for mental and nervous disorders, and epilepsy from many aspects. Tickets for the annual dinner may be obtained from the secretary, 11, Chandos Street, W.1.

Order of St. John of Jerusalem

The following appointments to and promotions in the Venerable Order of the Hospital of St. John of Jerusalem have been sanctioned by the King :—

As Knight.—Urban Marks, M.R.C.S.

As Commander.—Lieut.-Colonel Frank Romer, M.R.C.S., Sir Henry Gauvain, M.D., Francis Carr Bottomley, O.B.E., M.D.

As Officer.—Henry George Ramsbottom, L.R.C.P.E., Norman Harold Kettlewell, L.M.S.S.A., L.D.S., Ernest Joseph Burnett, M.B.E., M.R.C.P., David Henry Griffiths, M.R.C.S., Gwilym Llewelyn Pierce, L.R.C.P.E., Robert James Clarke, M.B., Lieut.-Colonel Edward Slade Goss, M.C., M.R.C.S., I.M.S., Francis Joseph Bach, M.D., John Craven Glen, L.R.C.P.E., Major Eben Stuart Burt Hamilton, M.C., M.B., Eric Hoerman, M.B., Andrew Croll, M.D., F.R.C.S.E., Edwin Francis White, F.R.C.S., Major Colin Wilson, M.B., R.A.M.C., Charles Paul Gaboury, M.D., Clarence John Archibald McKillop, M.D., Major Wilmot Edward Lenox Sparks, M.D., Lieut.-Colonel Ronald Herbert Candy, C.I.E., M.B., I.M.S., Lieut.-Colonel Norman Briggs, M.R.C.S., I.M.S., Mrs. Jane Pasley Hay Graham Brown, M.B.

Exhibits at the National Physical Laboratory

At the annual inspection of the laboratory on Tuesday last the special exhibits included photomicrographs and radiograms illustrating the structure of teeth. It has been found that there is a gradual decrease in the degree of calcification from the outer to the inner surface of the enamel. The inorganic constituent of the enamel has recently been proved to consist mainly of hydroxy-apatite, the crystals of which have an average dimension of 10–8 cm. and are associated into prisms containing perhaps half a million crystallites. The crystalline orientation deduced from radiographic appearances has been confirmed by the polarising microscope, which shows that within each prism, which extends from the dentine to the outer surface, there are in general two groups of crystallites, the one inclined at about 5° to the prism axis and the other at about 40°. The primary objects of this investigation, undertaken for the Medical Research Council, are to determine the structures of the enamel and of the underlying dentine and to observe how these structures vary with different types of teeth. Other exhibits of medical interest included apparatus designed for testing the accuracy of the colour of standardised tubes used in hæmoglobinometry and apparatus for testing the accuracy of glass butyrometers used in determining the percentage of fat in milk.

Medical Diary

July 3 to July 8

SOCIETIES

ROYAL SOCIETY OF MEDICINE, 1, Wimpole Street, W.1.

TUESDAY.—5 P.M., annual meeting.

THURSDAY.

Surgery.—8.30 P.M., Dr. D. W. G. Murray (Toronto): Heparin in Thrombosis and Embolism; Venous Grafts in Blood-vessel Surgery. Film: the formation of a thrombus.

EDINBURGH MEDICO-CHIRURGICAL SOCIETY.

WEDNESDAY.—8.30 P.M. (at the hall of the British Medical Association, 7, Drumsheugh Gardens), Mr. Laurence O'Shaughnessy: Surgical Revascularisation of the Heart.

LECTURES, ADDRESSES, DEMONSTRATIONS, &c.

BRITISH POSTGRADUATE MEDICAL SCHOOL, Ducane Road, W.12.

TUESDAY.—4.30 P.M., Sir Arthur Hall: Meningitis and Acute Infections of the Central Nervous System.

WEDNESDAY.—NOON, clinical and pathological conference (medical). 2 P.M., Prof. J. H. Dible: The Pathology of Liver Disease. 3 P.M., clinical and pathological conference (surgical).

THURSDAY.—2.15 P.M., Dr. Duncan White: radiological demonstration. 3.30 P.M., Dr. A. A. Moncrieff: Hygiene of the Newborn Child.

FRIDAY.—2 P.M., clinical and pathological conference (obstetrics and gynæcology). 2.30 P.M., Mr. J. B. Hume: Hernia and its Treatment.

Daily, 10 A.M. to 4 P.M., medical clinics, surgical clinics and operations, obstetrical and gynæcological clinics and operations.

ST. GEORGE'S HOSPITAL, S.W.1.

THURSDAY.—5 P.M., Dr. A. B. Stokes: psychiatric demonstration.

HOSPITAL FOR SICK CHILDREN, Great Ormond Street, W.C.1.

THURSDAY.—2 P.M., Dr. Wilfred Sheldon: Cow's Milk and its Modification in Infant Feeding. 3 P.M., Mr. Eric Lloyd: Diseases of the Hip-joint in Children.

Outpatient clinics daily at 10 A.M. and ward visits at 2 P.M.

FELLOWSHIP OF MEDICINE AND POSTGRADUATE MEDICAL ASSOCIATION, 1, Wimpole Street, W.1.

MONDAY to SATURDAY.—All Saints' Hospital, Austral Street, West Square, S.E.11, afternoon course in urology.

Appointments

BRITTON, C. J. C., M.D. N.Z., pathologist to the Samaritan Free Hospital for Women, N.W.1.

BURKITT, DENIS, F.R.C.S.E., resident surgical officer at the Prince of Wales's Hospital, Plymouth.

CLARKSON, J. R., B.Sc. Lond., consulting physicist to the Royal Northern Hospital, N.7.

COGSWELL, A. P. L., M.B. Lond., assistant deputy coroner for Central London.

HAMILTON, ALISON M., M.B. Edin., assistant bacteriologist in the public health laboratory, King's College, Newcastle-on-Tyne.

KANDER, H. S., M.R.C.S., registrar to the ear, nose, and throat department, Queen Mary's Hospital for the East End, E.15.

LAMBERT, V. F., Ch.M. Manc., honorary assistant aural surgeon to the Manchester Royal Infirmary.

LYTH, CONSTANCE, M. F., M.B. Manc., resident medical officer at the Royal Manchester Children's Hospital.

MEADOWS, S. P., M.D., M.R.C.P. Lond., honorary assistant physician to the Maida Vale Hospital for Nervous Diseases, W.9.

NATHAN, H. A., M.R.C.S., temporary assistant medical officer, Epsom.

NORRISH, R. E., F.R.C.S., assistant surgeon to the Albert Dock Hospital, E.16.

WEBB, W. L., M.B. Lond., temporary assistant medical officer of health for the city of Westminster.

Carshalton and District War Memorial Hospital.—The following have been appointed honorary medical officers :—

BLOOM, HAROLD, M.R.C.S.;
DRURY, E. W., M.B. Leeds; and
MAITLAND, H. L. C., Ch.M. Sydney.

Glasgow Corporation.—The following have been appointed assistant medical officers to the police force :—

BLACK, JOHN, M.B. Glasg.;
FITZ-SIMONS, A. B., M.B. Belf.; and
WALKER, R. N., M.D. Glasg.

Examining Surgeons under the Factories Act, 1937: Dr. E. C. HARBOTTLE (Montrose District, Angus); Dr. R. C. B. HALL (Llansawel District, Carmarthen); Dr. A. R. MCWHINNEY (Stratford-on-Avon District, Warwick); Dr. D. W. D. MACLAREN (Golspie District, Sutherland).

Vacancies

For further information refer to the advertisement columns

Aberdeen Royal Infirmary.—Asst. M.O. in X-ray and radium depts., £350.

Beckenham, Bethlem Hosp., Monks Orchard, Eden Park.—**Res. H.P.**, at rate of £150.

Belfast, Forster Green Hosp., &c., Fortbreda.—H.P., at rate of £150.

***Birmingham City.*—Jun. asst. M.O. for Rubery Hill and Hollymoor Divisions, £350.**

***Bristol City and County.*—Asst. M.O.H., £500.**

Bristol Royal Infirmary.—Res. med. appts., at rate of £150–£80.

British Hospitals Association, 12, Grosvenor Crescent, S.W.1.—Secretary, £1000.

British Postgraduate Medical School, Ducane Road, W.12.—First asst. in dept. of medicine, £300 to £600.

British Red Cross Society Clinic for Rheumatism, Peto Place, N.W.1.—Hon. neurologist.

Burnley, Victoria Hosp.—H.P., at rate of £150.

Cambridge, Addenbrooke's Hosp.—**H.S. and H.S.** to spec. depts., each at rate of £130.

Cardiff, King Edward VII Welsh National Memorial Association. Res. M.O. for Glan Ely Hosp., £350.

***Chester City Hosp.*—Res. M.O., £200.**

***Chesterfield and North Derbyshire Hosp.*—Cas. O. and fracture H.S., at rate of £225.**

Coventry and Warwickshire Hosp.—Res. M.O., £300.

***Dagenham Borough.*—Deputy M.O.H., £600,**

Derby, Derbyshire Royal Infirmary.—H.S. to ear, throat and nose dept., £150.

Dewsbury County Borough.—Deputy M.O.H. and deputy school M.O., £600.

Dewsbury and District General Infirmary.—Sen. H.S. and second H.S., £200 and £150 respectively.

Dover, Royal Victoria Hosp.—Second R.M.O., £140.

East Ham Corporation.—Assistant M.O.H., £500.

East Suffolk, County of.—Joint appointment of M.O.H., £800.

Eastbourne, Royal Eye Hosp., Pevensey Road.—H.S., at rate of £100 and £175.

Elizabeth Garrett Anderson Hosp., Euston Road, N.W.1.—Asst. pathologist, £250. Med. reg., £100.

Essex County Council and Thurrock Urban District Council.—Asst. county M.O.H., £700, asst. county M.O.H., and asst. M.O.H., £500.

Glasgow Western Infirmary.—Asst. radiologist, £400.

Gloucestershire Royal Infirmary, &c.—**Asst. to radiological dept., £500.**

Guy's Hosp., S.E.1.—Astley Cooper studentship, £130.

Hampstead General Hosp., Haverstock Hill, N.W.3.—H.S. and H.P., each at rate of £100.

Hôpital et Dispensaire Français, Shaftesbury Avenue, W.C.2.—Anæsthetist, £25.

Hosp. for Consumption and Diseases of the Chest, Brompton, S.W.3.—**H.P., at rate of £50.**

Hounslow Hosp.—H.P. and cas. O., at rate of £100.

Huddersfield Royal Infirmary.—H.S. to abnormal maternity dept., at rate of £150.

Ilford, King George Hosp.—Res. M.O., £150.

Ipswich, East Suffolk and Ipswich Hosp.—Radiotherapist, £600.

***Keighley and District Victoria Hosp.*—First and second res. M.O.'s, at rate of £160 and £120 respectively.**

Kensington County Hosp., Wolverton Avenue.—Res. asst. M.O., at rate of £250.

***Kent Education Committee.*—Dental surgeon, £500.**

Kidderminster and District General Hosp.—Sen. and jun. H.S., at rate of £150 and £100 respectively.

King Edward Memorial Hosp., Ealing.—Cas. O. and deputy res. M.O., at rate of £225.

***Kingston County Hosp., Wolverton Avenue.*—Res. asst. M.O., at rate of £250.**

Leeds, St. James's Hosp.—Res. surg. O., £350.

Lincoln County Hosp.—Jun. H.S., at rate of £150.

Liverpool Royal Children's Hosp., Myrtle Street.—Med. reg., £150. Also surg. reg., at rate of £150.

***Liverpool School of Tropical Medicine.*—Lecturer in parasitology, £700.**

London Chest Hosp., Victoria Park, E.2.—Med. reg., £175.

London County Council.—Part-time obstet. and gynæcol., £600.

***London Hosp., E.1.*—Medical first asst. and registrar, £300.**

London Lock Hosp., 283, Harrow Road, W.9.—Surg. reg., £100.

Manchester, Crumpsall Hosp.—Res. surg. O., £400.

Manchester Royal Infirmary.—Radiologist for X-ray diagnostic work, £1000. Res. surg. O., £200. Also med. reg. to out-patient dept., at rate of £150.

Mansfield and District General Hosp.—H.S., at rate of £150.

Middlesbrough, North Riding Infirmary.—Cas O., at rate of £150.

Middlesex Hosp., W.1.—Surg. reg., £300.

National Hosp., Queen Square, W.C.1.—H.S., £100.

Newcastle General Hosp.—H.P.'s and H.S.'s, each at rate of £150.

Newcastle-upon-Tyne Throat, Nose and Ear Hosp.—H.S., £150.

North Middlesex County Hosp., Silver Street, Edmonton, N.18.—Jun. asst. M.O., at rate of £250.

Nottingham City Mental Hosp.—Sen. asst. M.O., £580.

Nottingham General Hosp.—H.P., at rate of £150.

***Oldham, Municipal Hosp.*—Res. asst. M.O., at rate of £200.**

Oxford, Lady Margaret Hall.—John Malcolm Mitchell scholarship, £80.

Plymouth City.—Public vaccinator.

Pontefract General Infirmary and Hydes Hosp.—**Sen. res. surg. O., at rate of £175 to £200.**

Portsmouth, St. James Hosp. for Nervous and Mental Disease, Milton.—Locum tenens asst. M.O., 7 guineas a week.

Preston and County of Lancaster Royal Infirmary.—H.P., £150.

Princess Elizabeth of York Hosp. for Children, Shadwell, E.1.—Cas. O., at rate of £125.

Queen Charlotte's Maternity Hosp., Marylebone Road, N.W.1.—Sixth M.O. for antenatal dept.

Reading, Royal Berkshire Hosp.—H.S. to spec. depts., at rate of £150.

Romford, Oldchurch County Hosp.—Asst. res. surg., £350.

Romford Isolation Hosp.—Jun. asst. M.O., £250.

Royal Cancer Hosp., Fulham Road, S.W.3.—Res. M.O., £200.

Royal National Orthopædic Hosp., 234, Gt. Portland Street, W.1.—Surg. reg. for country branch, £300. Also two H.S.'s for country branch, each at rate of £150.

***Royal Naval Medical Service.*—Medical officers.**

Royal Northern Hosp., Holloway, N.7.—H.P. and obstet. H.S., each at rate of £70.

St. Mark's Hosp. for Cancer, &c., City Road, E.C.1.—H.S., at rate of £120.

St. Paul's Hosp. for Urological and Skin Diseases, Endell Street, W.C.2.—Hon. urological and cancer registrar. Hon. asst. surgeon in urological dept. Also radiologist, £100.

St. Thomas's Hosp., S.E.1.—Hon. director of radiotherapy dept. Also two physicians in charge of outpatients.

Salisbury General Infirmary.—H.S., at rate of £125.

Sheffield Royal Hosp., West Street.—Res. surg. O., £200.

Sheffield Royal Infirmary.—Res. H.S. to ophthalmic dept., at rate of £80–£120.

Shrewsbury, Royal Salop Infirmary.—Res. H.S., at rate of £160.

South London Hosp. for Women and Children, Clapham Common, S.W.4.—H.S., at rate of £100.

Southampton, Borough Isolation Hosp.—Res. M.O., £350.

Southampton County.—Asst. county M.O., £600.

Southampton County Borough.—Deputy M.O.H., £720.

Sunderland Royal Infirmary.—H.P., at rate of £120.

Victoria Hosp. for Children, Tite Street, Chelsea, S.W.3.—H.P. and H.S., at rate of £100. Also cas. O., at rate of £200.

***Walthamstow Borough.*—Asst. obstet. res. M.O. for Maternity Hosp., £200.**

West End Hosp. for Nervous Diseases, Gloucester Gate, N.W.1.—Two res. H.P.'s, each £125.

***West London Hosp., Hammersmith, W.6.*—Chief clin. asst. in X-ray (diagnostic) dept., £125.**

Worcester County and City Mental Hosp., Powick.—Asst. M.O., £350.

Medical Referee under the Workmen's Compensation Act, 1925, for the County Court District of Barnsley (Circuit No. 13). Applications should be addressed to the Private Secretary, Home Office, Whitehall, London, S.W.1, before July 16. Also for the Dumbarton Sheriff Court District (Sheriffdom of Stirling, Dumbarton, and Clackmannan). Applications to the Private Secretary, Scottish Office, Whitehall, London, S.W.1, before July 17.

The Chief Inspector of Factories announces vacancies for Examining Factory Surgeons at Ashby-de-la-Zouch (Leicester), Kenninghall (Norfolk) and Fenny Stratford (Buckingham).

Births, Marriages and Deaths

BIRTHS

ANNING.—On June 25, at Leeds, the wife of Dr. R. M. Anning, of Ripon—a daughter.

BARTON.—On June 26, at Welbeck Street, to Dr. Mary Barton, the wife of Dr. Douglas E. Barton, of Morden—a daughter.

CAPPS.—On June 19, at Park Square East, London, N.W.1, the wife of Mr. F. C. W. Capps, F.R.C.S.—a daughter.

COATES.—On June 22, at Westminster Hospital, the wife of Dr. Richard Coates, of Edenbridge—a son.

DILL-RUSSELL.—On June 25, at Nicosia, Cyprus, the wife of Dr. P. W. Dill-Russell—a daughter.

EVANS.—On June 23, at Tunbridge Wells, the wife of Dr. W. G. Evans—a daughter.

KAY.—On June 22, at Sylvan Avenue, Mill Hill, the wife of Dr. E. J. S. Kay, of Boreham Wood—a son.

KEITH.—On June 24, at Melton, Suffolk, the wife of Dr. W. Brooks Keith—a son.

ROBERTSHAW.—On June 20, at Douglas, Isle of Man, the wife of Captain G. M. Robertshaw, R.A.M.C.—a son.

MARRIAGES

KETTLE—DREW.—On June 24, at St. Paul's Church, Weston-super-Mare, Austin Braybrooke Kettle, M.D., to Dorothy Mary Drew.

LEEDHAM-GREEN—CALDWELL.—On June 23, at St. Peter's Church, Burnham, Bucks, John Charles Leedham-Green, F.R.C.S., to Gertrude Mary Somerville Caldwell, M.B.

DEATHS

HAYLOCK.—On June 23, at Droitwich, Sydney John Haylock, M.R.C.S., of Southbourne, Bournemouth.

N.B.*—*A fee of 7s. 6d. is charged for the announcement of Births, Marriages, and Deaths.

VALEDICTORY.—We part this week with the senior member of the staff, Mr. F. W. White, who has been editorial secretary since August 19, 1901. He has contributed to our columns many informative notes. His memory goes back to the Wakley tradition and many of our contributors are unknowingly indebted to his unrivalled knowledge of medical names and terms for their immunity from painful slips and omissions. All his colleagues on the staff are aware of their debt and wish him God-speed in his retirement.

NOTES, COMMENTS, AND ABSTRACTS

THE PHYSIOLOGY OF MARITAL INTERCOURSE

AN INQUIRY

BY J. R. GROOME, M.A., B.Sc. Oxfd

(*From the Department of Zoology and Comparative Anatomy, Oxford University*)

THREE married professional men, living in the south of England, undertook to keep accurate notes of their sex-life for 15 months. Much of the data so obtained is necessarily subjective; but it was hoped that accurate detail from a small source over a long period might be of greater value than replies to a general questionnaire. Wider verbal inquiries indicate some measure of agreement in matters which are susceptible to corroboration.

This inquiry was originally intended as a study of the prostate gland in young men; the ancillary findings cannot form a basis for comparison with the statistical data of Pearl (1925) on the frequency of coitus, or that of Engle and Shelesnyak (1934) on the menstrual cycle, as the method of approach is different, but they may be complementary to those works.

At the beginning of the inquiry the investigators were:—

1. Age 25, wife 26, married 2 years, 0 children.
2. Age 30, wife 32, married 6 years, 1 child.
3. Age 36, wife 33, married 10 years, 2 children.

All use contraceptives.

THE MENSTRUAL CYCLE

The average length of the menstrual cycle in the wives of these three men was 25·6 days, and the average number of copulations in each intermenstrual period was 6·2. From April to September the menstrual cycle occupied 26·3 days with 7·3 copulations; from September to April it occupied 25·1 days with 5·7 copulations. That is to say, throughout the summer there was an average of one copulation every 3·6 days, and throughout the winter one every 4·4 days.

Periods of desire seem to be infinitely variable, but the three women under consideration agreed fairly well. It seems in these cases that desire is at its lowest during the 6 or 7 days preceding menstruation; it rises steeply during menstruation and reaches a peak 2 days after menstruation has stopped. Desire then decreases slightly for 4 or 5 days; it increases again in the next 4 days and reaches a second, but less intense, peak. This second peak usually occurs 14 days after the beginning of the preceding menstrual period and is presumably associated with ovulation (Horrenbergen 1928). After this desire decreases, reaching its minimum a week before the beginning of the next menses.

This variation in desire is shown graphically and arbitrarily in the figure, with the copulations of no. 2 marked on the curve. A line has been drawn separating the curve into two portions of equal duration in each intermenstrual period. Where the curve is above this threshold line it represents a period of desire; where it is below the line a period of indifference.

During the 15 months of this inquiry there was an average per married couple of 70 copulations in the desire period, and 49 in the indifferent period. From April to September there were 4·6 copulations in the desire period and 2·6 in the indifferent period of each menstrual cycle; throughout the winter the figures were 3·0 in desire and 2·7 when indifferent. This, in conjunction with the greater frequency of coition, suggests that desire in women is more intense in warm weather, which agrees with the general evidence from the tropics.

The women also report an increase in the hip, waist and breast measurements six or seven days before menstruation begins, returning to normal when menstruation ends. This can hardly be comparable to the cyclical changes in the sexual skin of primates (Krohn and Zuckerman 1937, Zuckerman 1937), for in monkeys the swelling is in the follicular phase. It is, however, possible that there are similar metabolic changes, involving the utilisation of extraneous water. In women this increase, which is associated with sexual indifference, is doubtless a corollary of pseudopregnancy. Both pseudopregnancy and the indifferent phase are terminated by menstruation.

The fact that these women experience greatest desire at a time in the menstrual cycle when conception is unlikely may lend some support to Zuckerman's theory of the evolution of the family unit.

THE SEMEN

When rubber sheaths were used the volume of the ejaculate was measured. For the purposes of this inquiry an ejaculate of less than 3 c.cm. is called small, of 3–4 c.cm. medium, and of more than 4 c.cm. large. Ejaculates of medium volume were most common.

It was found that the amount of the ejaculate was not necessarily proportional to the length of the period of abstinence preceding it, although abstinence for 7 or more days usually ended in an ejaculate of more than 4 c.cm., and ejaculates of less than 3 c.cm. usually followed three copulations in the preceding 4 or 5 days. Volume was apparently unaffected by the common cold, but was much reduced after a fever.

The semen may contain solid bodies known as prostatic concretions, which are small concentrically marked grains staining with iodine, apparently formed in the alveoli of the prostate. Sometimes they are partly calcified and are then called prostatic sand. Large squamous cells of unknown origin may also be found in semen. These bodies are collectively referred to as debris. I am indebted to Dr. J. R. Baker and his assistants for assessing the debris and counting sperms in samples from one investigator (see Baker, Ranson and Tynen 1937). They found that washed sheaths must be used if the debris is to be assessed accurately, as the concretions are almost indistinguishable from the starch grains with which sheaths are dusted.

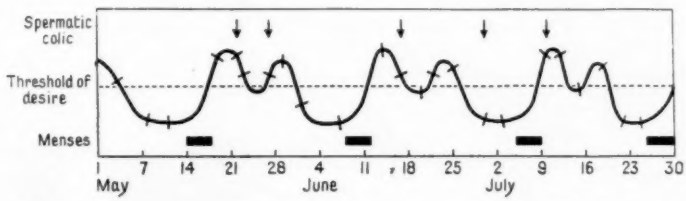
The amount of debris is very variable in different people and also in the same person at different times. A large amount of debris is not associated with a large ejaculate, and is therefore not produced as a result of high internal pressure in the ducts and glands; nor is it associated with a small ejaculate, so that it does not seem to indicate an effort by the glands to produce a certain minimum of secretion. A large amount of debris is most usually found in the normal medium-sized ejaculate.

One investigator (no. 2) normally produced 182 million sperms per c.cm. of semen. In August he

contracted a streptococcal infection akin to scarlet fever. The fever lasted a week, and three weeks later, with four ejaculations intervening, the fifth ejaculation contained so few sperms and was so small in volume that the sample was useless for experimental work. Unfortunately no accurate assessment of the number of sperms was made. It seems, however, that a febrile illness may result in temporary sterility.

In the following winter this same investigator, aged 30, endeavoured to induce sterility artificially. His body-temperature taken in the groin was 36·6° C. In the morning before getting out of bed his average scrotal temperature was 34·3° C.; in the evening it was 33·0° C. For the 5 weeks of the experiment he wore, during the day only, a suspensory bandage containing three layers of Thermogene wool. This raised the evening temperature of the scrotum to 35·4° C. The morning temperature was also found to be higher than normal, presumably as a result of increased blood-supply, the average being 35·3° C.

If spermatogenesis is slowed down or stopped the number of sperms in the semen will fall in proportion to the number of ejaculations that have taken place since the inhibitory condition started. Conversely, when spermatogenesis is restarted or its rate increased the number of sperms in the semen will probably increase in proportion to the time between such restarting or increase and ejaculation.



Arbitrary curve showing periodic variations in desire of the wife of no. 2. Copulations are marked on the curve.

After 9 days of the experiment, during which there had been three ejaculations, the number of sperms had fallen from 182 million to 117½ million per c.cm. of semen. After a further 15 days, and four ejaculations, it had fallen to 52¼ million per c.cm. which was the lowest figure obtained. This was rather a small ejaculate, in which normally sperms are relatively more numerous, and represented an ejaculation of only 115½ million sperms; whereas this man's normal total is 637 million. After a further 10 days and two ejaculations the number of sperms rose to 244 million per c.cm. and the next ejaculate in 3 days' time gave 215 million per c.cm Throughout the experiment the epididymis on both sides appeared to be enlarged, but the increase was presumed to be entirely vascular.

It seems from this experiment that an average increase in scrotal temperature of 1·7° C. is sufficient to discourage spermatogenesis for a short time. After 4 weeks the testes become acclimatised and spermatogenesis proceeds more actively than usual. Possibly more conclusive results could be obtained in the summer. As bed-clothes keep the scrotum more than 1° C. warmer than trousers, it is possible that a non-febrile disability, such as an accident which keeps the patient in bed, may result in a temporary reduction of fertility.

THE MALE CYCLE

Two of the investigators experience considerable discomfort in the lower abdomen and region of the rectum from time to time. The condition will normally disappear in a few hours, but may recur the next day or in two days' time. It is relieved almost at once by copulation. The frequency of urination is increased when this sensation is present but it is not affected by the condition of the bowel. It was most marked in April, May and June. It seems probable that this discomfort originates in the prostate, but I do not know whether it is normal or pathological. The youngest of our three investigators never experienced it; and on wider inquiry most of the men who were asked either did not know it or would not admit to it. It may only arise in prostates with a tendency to produce debris; but it was not as a rule associated with an ejaculate containing a large amount of debris.

Prostatic discomfort was usually evident in investigators 2 and 3 at intervals of from 28 to 10 days, the mode being 19 days. There was, however, one gap of 59 days and another of 71 days in which the discomfort was not evident. These gaps are not incompatible with an ill-defined cycle of 19 days, and it is suggested that they represent three and four periods respectively, which were missed, in prostates normally experiencing a cycle of this length.

Information was also supplied by Dr. X, aged 38, who from the age of 30 had experienced fairly acute discomfort in the region of the prostate at regular fortnightly intervals—in fact, at one time he had come to expect it on alternate Thursdays. He produces debris in his semen, and confirms the symptoms, with the exception that in his case the discomfort was not relieved by copulation. Dr. X found that the discomfort ceased when he took to riding on horseback and did not return when he gave up this exercise for some months. At the end of this inquiry one of the investigators bought a horse and the symptoms ceased when he rode; but they returned when the horse went lame and could not be ridden. It has been suggested that this recurrent discomfort may be due to a vascular congestion, which is dissipated by what amounts in effect to massage; it should therefore be mentioned that investigators 2 and 3 and Dr. X have no hæmorrhoidal tendencies.

All three investigators reported a less acute sensation, which gives the impression of pressure in the epididymides or vasa deferentia or in both. It may be bilateral or unilateral, and when present in the epididymis this organ appears to enlarge. It was first noticed by one of the investigators, before his marriage, as a very acute pain in the vasa deferentia. It would occur after periods of ungratified sexual excitement, such as a day spent in the company of his fiancée. Since marriage, in this case, as with the other investigators, this so-called spermatic colic has appeared as a mild discomfort at intervals.

Spermatic colic is often associated with an ejaculate containing much debris; it sometimes accompanies prostatic discomfort; only once in the present investigation was it noticed to be associated with a small volume of ejaculate; it may arise on two

successive days in spring and summer, or with an interval of as much as 52 days in winter. Spermatic colic does not always follow abstinence, as might be expected if it is due to pressure in the ducts; in fact it often comes on at times when intercourse is frequent, but it is not possible to say that one is the cause of the other. In one case it was noted that spermatic colic was felt 18 times in the wife's period of desire and 11 times in the indifferent period. In the summer months, when desire was more apparent, it was noted 9 times in the desire period and only 3 times in the indifferent period, which suggests that its cause may not be entirely physiological.

Inquiry disclosed that spermatic colic, though not universal, is a much commoner symptom than prostatic discomfort. It is evident that the two phenomena are not associated.

A prostatic cycle, probably under the influence of the pituitary body and the testes, is not an impossibility in view of recent work on mammalian intersexuality.

SUMMARY

The marital sex-life of three young professional men was investigated for 15 months. Sexual activity was more apparent in summer than in winter.

Certain prostates seem to undergo cyclical changes occupying 2–3 weeks and involving physical discomfort. This cycle may only be noticeable in prostates producing debris; it may be pathological. Riding a horse was found to allay the symptoms.

Spermatic colic is often associated with the presence of prostatic debris, but the ultimate cause may be psychological, as the presence of debris is not universal.

Spermatogenesis is probably checked by fever. It was also checked by raising the temperature of the testes artificially, but proceeded normally when these had become acclimatised to the new conditions.

I am indebted to my three anonymous collaborators and to Dr. J. R. Baker for much helpful comment.

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MEDICAL ORATIONS

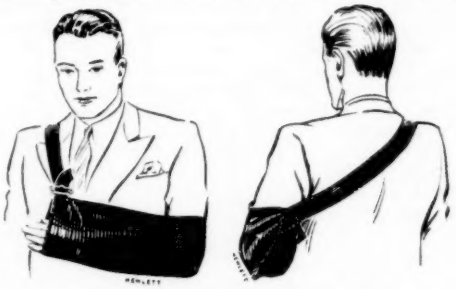
A REPUTATION as a medical orator is an unhappy possession, for at least three or four times a year its possessor must face an audience which demands an exhibition of oracular wisdom. In his "March of Medicine" (London: Humphrey Milford, Oxford University Press. 1938. Pp. 280. 12*s*. 6*d*.) Dr. Lyman Wilbur of California has collected 29 of these Delphic utterances delivered by him between 1913 and 1937. They are quite characteristic. The glowing past and radiant future of our profession are painted in the routine colours. No doubt this is what congresses like, or why should Dr. Wilbur have been called on time and again? These addresses could certainly hurt nobody's feelings, but they will leave most readers cold.

SULPHANILAMIDE IN TULARÆMIA

Dr. Henry G. Hadley, of Washington, D.C., informs us that he has noted clinical improvement in a patient with tularæmia treated with sulphanilamide. The patient, a white female, aged 29, was seen on Nov. 28, 1938, having a shallow ulcer on the right index finger with a greyish slough and associated with enlargement of the epitrochlear and axillary glands. The finger had been injured two weeks earlier while she was dressing a rabbit. The illness began four days later with sudden onset of chill and fever, and she was confined to bed for a week and treated for influenza. On Dec. 1 the serum gave a positive test for tularæmia, 1 in 27 dilution. Sulphanilamide gr. 30 was given daily from Dec. 4 to Dec. 8 and was discontinued temporarily because of a general eruption. It was started again as soon as the rash had disappeared, and from Dec. 22 to Jan. 4 she received gr. 30 daily. The enlargement of the glands had almost entirely subsided and the finger lesion had entirely healed by Jan. 4. During both periods of sulphanilamide therapy improvement was noted subjectively and objectively, and while it was discontinued the patient's condition remained relatively stationary.

AN ARM-SLING

C. J. HEWLETT & SON, LTD., send us the accompanying sketch of the "Mead" adjustable arm-sling. The advantages claimed for it are: (1) it can be used for



either arm; (2) the weight is carried by the shoulder and not by the neck; (3) it is readily adjustable by means of a non-slipping buckle; and (4) it is light and washable. Messrs. Hewlett's address is 34, Charlotte Road, London, E.C.2.

MANUSCRIPTS AND ENGRAVINGS

AMONG the manuscript treasures which Messrs. Sotheby are to offer for sale next month is a thirteenth-century copy of Albuhasim De Chirurgia, bound up with other medical works and illuminated with miniatures and drawings of instruments. It affords an example of the fleeting character of human fame, for it is by the beauty of the setting alone that Albuhasim's work has survived the lapse of ages. Great in his generation he now lives only by the patient and devoted work of an unnamed English scribe. The same train of thought is suggested by Messrs. Suckling's catalogue of engraved portraits of scientists. In their lives or after their deaths these men climbed at least the first slopes of the hill of Fame, yet to us their representations are chiefly valued not for the memorial of what they accomplished but for the beauty and vigour of the—often unknown—artist's work.

REPRINT OF HIPPOCRATES

"Adams, of Banchory (a little Aberdeenshire village), was not only a good practitioner and a skilful operator but he was an excellent naturalist. This is by no means an unusual or remarkable combination, but Adams became in addition one of the great scholars of the profession. He had a perfect passion for the classics. . . . He translated the works of Paulus Aegineta, the works of Hippocrates, and the works of Aretaeus . . . monuments of the patient skill and erudition of a Scottish village doctor. . . ." So wrote Osler in one of those papers in which he delighted to praise our forefathers. The Sydenham Society published Adams's translation of Hippocrates in 1849, and now, nearly a century later, his work has been reprinted by Baillière, Tindall and Cox in a neat volume (The Genuine Works of Hippocrates. London. 1939. Pp. 384. 13*s*. 6*d*.) which reproduces the text with few modifications, but omits much of Adams's notes and illustrations.